Motion Sickness

Timothy C. Hain, MD

Motion sickness is the nausea, disorientation and fatigue that can be induced by head motion. The first sign is usually pallor. Yawning, restlessness and a cold sweat forming on the upper lip or forehead often follow. As symptoms build, an upset stomach, fatigue or drowsiness may occur. The final stages are characterized by nausea and vomiting.

Motion sickness is common and normal. Nearly anyone can be made motion sick by an appropriate stimulus, except for individuals with no vestibular system (William James). In a large study done in India, the prevalence of motion sickness was about 28%, and females were more susceptible (27%) were more susceptible than males (16.8%). Individuals with more active occupations are less susceptible (Sharma, 1997). In medical transport personnel, 46% of personnel reported nausea and 65%, the sopite syndrome (sleepiness caused by motion). (Wright, 1995)

According to Benson, nearly 100% of occupants of life rafts will vomit in rough seas. 60% of student aircrew members suffer from air sickness at some time during their training. For vertical motion (heave), oscillation at a frequency of about 0.2 hz is the most provocative. Motion at 1 Hz is less than 1/10th as provocative. About 7% of seagoing passengers report vomiting during a journey (Lawther and Griffin, 1988). Women are more sensitive to motion than men, by a ratio of about 5:3. Transportation devices with unusual sensory stimuli, such as "tilting

What Causes Motion Sickness ?

In order for the body to determine where it is at all times, the brain combines visual information, touch information, inner ear information, and internal expectations. Under most circumstances, the senses and expectations agree. When they disagree, there is conflict, and motion sickness can occur.

For example, consider the situation when one is reading in the back seat of a car. Your eyes, fixed on the book, say that you are still. However, as the car goes over bumps and accelerates/decelerates, your ears disagree. This is why motion sickness in this situation is common.

Acquired susceptibility to motion sickness occurs occasionally. Persons with an inner ear disturbances, especially a recent one, may be intolerant to activity in general. People with migraine are apt to get motion sick. Persons with rare, central nervous system disorders of the part of the brain that processes signals from the inner ear may also be unusually susceptible to motion sickness. Certain individuals who are constitutionally susceptible to motion sickness and can develop sea sickness on ships, and a prolonged land sickness, when they get off the ship. This rare disorder is called "mal de debarquement", which is French for "bad getting off the ship". Persons with unusually good vestibular function may be more susceptible to motion sickness than others (Gordon et al, 1996).

Migraine is a definite risk factor for motion sickness, with roughly a 5 fold greater incidence than non-migraineurs. Female gender and youth is also a risk factor. In women, days 9-15 appear to have a higher incidence of nausea (Ramsay, 1994).

Experimentally, motion-sickness can be eliminated in dogs by surgically removing part of the brain (the nodulus, according to Bard). Motion sickness is sometimes associated with prolonged vestibular responses (Hoffer et al. 2003).

Treatment of Motion sickness:

There are essentially three strategies to treatment of motion sickness:

- Behavioral (avoidance, mental activities)
- Medication (conventional, alternative)
- Stimulation (alternative)

Behavioral Strategies for Motion Sickness

- In the car: sit in the front seat or drive.
- Aboard a ship: stay toward the middle and look at the horizon. Avoid ship travel if possible. Stay out of small tight places where you can't see the horizon.
- On the airplane: ask for a window seat. The front of the plane may be preferable, as it is usually less noisy.
- For cars: It may be helpful to mentally rehearse a trip route as familiarity and anticipation is sometimes helpful.
- Face leeward (so if you vomit, it gets blown away from the ship, not into it).
- Eat bland foods -- crackers and bread, or bananas, rice, applesauce and toast.

Medication for Motion Sickness

Most medications for motion sickness need to be taken at least 30 minutes before exposure to the activity that can cause the problem. Persons with glaucoma or prostate problems should not take most of these medications unless so advised by their doctor.

- *Meclizine (Antivert, Bonine)*. In the antihistamine family. Can cause drowsiness. Like other most other medications, it is best to take these before motion stimulation.
- *Dimenhydrinate* (Dramamine). Similar to meclizine. Liquid forms are available for children 2 years of age or more.
- *Cyclizine* is similar to meclizine. It is suitable for children 6 years of age or older as well as adults. It is most useful in situations involving short trips (e.g. automobile).
- Haldol, Thorazine -- these anti-psychotic drugs have dopamine blocking activity which is useful for blocking nausea as well as stimulating stomach motion which helps clear food from the digestive tract.
- *Promethazine*. This drug is one of the most effective available for motion sickness. One dose lasts up to 8 hours. Like the other drugs, it can cause drowsiness.
- *Diazepam (valium)* and related medications such as lorazepam and klonazepam. While these drugs are not traditionally used for motion sickness, some people find them useful in small amounts. These medications are very helpful for a related condition, MDD.
- Scopolamine patches -- these patches are sometimes very helpful. They are a time release form of an anticholinergic medication, scopolamine. Scopolamine is also available in pill format (usually given for irritable bowel)
- Zofran and other serotonin-family antinausea drugs -- these are powerful anti-nausea medications. They do not prevent motion sickness but they may prevent emesis.

- *Other medications.* Verapamil (a calcium channel blocker), phenytoin and carbamazepine (sodium channel blocker) are also sometimes useful. Buspirone (Buspar), and Beta-histine (Serc) may also be helpful.

Medications for nausea and vomiting

Treatment of motion sickness differs from treatment of nausea and vomiting. A discussion of emesis can be found here.

Stimulators for Motion sickness

There are several devices that purport to reduce motion sickness through stimulation of various places on the body (usually the wrist). These include "Sea Bands" and "Relief Band", among others. These devices may be placebo's, but so what.

Alternative medications

There are numerous "alternative" remedies for motion sickness. The most popular are Ginger derivatives, such as ginger tea, powdered ginger capsules, and even raw ginger between the teeth.

See also: http://www.sciam.com/askexpert_question.cfm?chanID=sa005&articleID=00007F4B-D6FD-1E4B-967D809EC588EEDF

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Are there any prescription treatments for motion sickness?

Motion sickness is a feeling of nausea that occurs with movement. Transdermal scopolamine (brand name Transderm-Scop) is a prescription medicine that's very effective for preventing motion sickness. It's a patch that you wear behind your ear. Your body absorbs the drug from the patch. Left in place, each patch works for up to three days.

Studies show that Transderm-Scop can decrease motion sickness in up to 75 percent of people who use it. Its most common side effects include dry mouth, constipation, and drowsiness. Still, it generally causes less drowsiness than over-the-counter motion sickness drugs.

Only adults should use Transderm-Scop because there's no information about the safe use of this drug in children under age 18.

Besides the patch, there are prescription drugs you can take orally or rectally for moderate to severe nausea and vomiting caused by motion sickness. These drugs include promethazine (Phenergan) and prochlorperazine (Compazine).

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Motion sickness

How to help your patients avoid travel travail

Paul M. Gahlinger, MD, PhD

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CME learning objectives

- To recognize the signs and symptoms of motion sickness
- To learn about the common risk factors of motion sickness
- To understand the appropriate medications for motion sickness

This page is best viewed with a browser that supports tables

Preview: Motion sickness is a common response to real and perceived movement through the environment. Although this malady is often joked about, symptoms can be serious and, for some people, incapacitating. Dr Gahlinger describes the physiology of motion sickness, discusses the mechanism and efficacy of common remedies, and offers recommendations for appropriate management.
Gahlinger PM. Motion sickness: how to help your patients avoid travel travail. Postgrad Med 1999;106(4):177-84

Motion sickness has been well known for thousands of years. Ancient seafaring nations were very familiar with this malady. In fact, nausea is derived from the Greek word *naus* (ship). Motion sickness has become increasingly prevalent with development of the many forms of vehicular travel, amusement park rides, and ever more dizzying visual stimuli. Various names give an indication of this ailment's many causes: seasickness, airsickness, car sickness, train

sickness, amusement-park-ride sickness, camel sickness, motion-picture sickness, microscope sickness, flight-simulator sickness, and space-motion sickness. Surveys have found that car sickness occurs in 58% of children, space-motion sickness occurs in 50% of shuttle astronauts, and incapacitating airsickness occurs in 29% of airline pilots (1). Up to 100% of ship passengers become seasick under rough conditions (2).

Symptoms and susceptibility

Characteristically, motion sickness begins with epigastric discomfort, often described as "stomach awareness," which is usually accompanied by increased salivation, eructation, and a feeling of bodily warmth. With sustained exposure to the triggering stimulus, gastric emptying is inhibited (3) and symptoms progress to nausea, pallor, sweating and, eventually, vomiting or retching. Some researchers suggest that there is another, distinct syndrome of motion sickness that lacks these gastrointestinal complaints and is instead characterized by drowsiness, headache, apathy, depression, and generalized discomfort (4). It is quite likely that many people experience both syndromes to varying degrees.

The cause of motion sickness is generally considered to be a mismatch of vestibular and visual sensations. However, actual movement of the body is not necessary to produce symptoms. Purely visual stimuli, such as those from flight simulators, video games, panoramic movies, or even the movement of slides under a microscope, can produce symptoms more effectively than does actual physical motion (5). The degree of motion sickness appears to be directly related to how well the visual stimulus simulates motion. For example, high-quality military flight simulators are reported to elicit symptoms in 40% to 70% of pilots in training (6).

Not everyone is susceptible to motion sickness. Children younger than 2 years of age are rarely affected, but susceptibility rapidly increases with age, peaking between 4 and 10 years, then gradually declining (7). Females tend to be more susceptible than males, regardless of age. Recent ingestion of food, particularly dairy products and foods high in sodium, protein, or calories, has been associated with increased susceptibility (8). A high level of aerobic conditioning further increases susceptibility, perhaps by increasing parasympathetic tone. Use of oral contraceptives also enhances susceptibility, and women are especially vulnerable during menses or pregnancy (2). Anxiety and preexposure tendency to facial flushing or nausea correlate with subsequent motion sickness (9). However, other personality factors have not been clearly associated with susceptibility (4).

Physiology

In humans, movement through the environment is inferred by three principal sensory systems: the visual sense and the two components of the vestibular system of the inner ear. This system includes the semicircular canals, which detect angular acceleration, and the otolith organs, which sense

translational acceleration. (Other proprioceptive sensations have a minor contribution to motion sickness.) Earlier theories that motion sickness is produced by vestibular overstimulation have been discounted. It is now fairly widely accepted that motion sickness is caused by conflicting inputs between the visual and vestibular systems, or between the two vestibular systems, and comparison of those inputs with the individual's expectations derived from previous experience (5).

Motion sickness occurs most commonly with acceleration in a direction perpendicular to the longitudinal axis of the body, which is why head movements away from the direction of motion are so provocative. Vertical oscillatory motion (appropriately called heave) at a frequency of 0.2 Hertz is most likely to cause motion sickness (7). (This frequency would be experienced onboard a ship with a roll rate of 5 seconds.) The incidence of motion sickness falls quite rapidly at higher frequencies. The apparent protection at these higher frequencies helps explain why motion sickness is commonly experienced on camelback, but not on horseback, and onboard ships, but not while windsurfing.

Adaptation to the sensory conflict is variable, and motion sickness tends to subside after 36 to 72 hours of continuous exposure. However, on return to the preexposure environment, symptoms can recur (*mal de débarquement*) until readaptation takes place (7).

Treatment

Nausea and vomiting are the most common complaints of motion sickness and are mediated by central neurotransmitters. In response to visual and vestibular input, increased levels of dopamine stimulate the medulla oblongata's chemoreceptor trigger zone, which in turn stimulates the vomiting center within the reticular formation of the brain stem. The vomiting center is also directly stimulated by motion and by high levels of acetylcholine. Therefore, most drugs that are used to prevent or ameliorate motion sickness target these neurotransmitters.

Common motion sickness drugs fall into three classes: antidopaminergics, anticholinergics, and antihistamines (table 1). Sympathomimetic agents are often added to counter the somnolent side effects. However, the precise action of these medications in preventing motion sickness is not known (10).

Table 1. Common pharmacologic therapies for motion sickness

Drugs	Dosage
Antidopaminergics	
Promethazine HCl (Anergan, Phenergan)	Adult: 12.5-25 mg q24h PO, PR, IM, or IV Child: 1/2 adult dose PO, PR, IM,

	or IV
Metoclopramide HCl*	Adult: 10 mg qid PO, IM, or IV
Anticholinergic	
Scopolamine HBr (Transderm-Scop)	Adult: 1 patch q72h
Antihistamines	
Meclizine HCl	Adult: 25-50 mg q24h PO
Diphenhydramine HCl	Adult: 50-100 mg q4-6h PO, IM, or IV (maximum, 400 mg/d) Child 6-12 yr: 25 mg q4-6h PO (maximum, 300 mg/d) ***or*** 1 mg/kg tid IM (maximum, 300 mg/d)
Dimenhydrinate	Adult: 50-100 mg q4-6h PO or IM (maximum, 400 mg/d) Child 6-12 yr: 25-50 mg q6-8h PO (maximum, 150 mg/d) ***or*** 1.25 mg/kg qid IM or IV (maximum, 300 mg/d) Child 2-6 yr: ≤25 mg q6-8h PO (maximum, 75 mg/d) ***or*** 1.25 mg/kg qid IM or IV (maximum, 300 mg/d)
Cyclizine (Marezine)	Adult: 50 mg q4-6h PO or IM (maximum, 200 mg/d) Child 6-12 yr: 25 mg q4-6h PO (maximum, 75 mg/d) ***or*** 1 mg/kg tid IM (maximum, 75 mg/d)
Buclizine HCl (Bucladin-S Softabs)	Adult: 50 mg q4-6h PO
Other	
Trimethobenzamide HCl*	Adult: 250 mg tid or qid PO ***or*** 200 mg tid or qid PR or IM Child 15-45 kg (33-99 lb): 100-200 mg tid or qid PO or PR Child <15 kg (<33 lb): 100 mg tid or qid PR

*Approved by US Food and Drug Administration as an antiemetic, but not specifically for motion sickness.

Antidopaminergics

The most effective antidopaminergic agent currently approved for motion sickness is promethazine hydrochloride (Anergan, Phenergan), a phenothiazine derivative with antihistamine, anticholinergic, and sedative effects. It is useful for both active and prophylactic treatment of motion sickness. Promethazine is available in tablet, syrup, suppository, and injection forms and has a duration of 4 to 6 hours. Metoclopramide hydrochloride is also commonly used, particularly if stomach distress is the predominate symptom.

Anticholinergics

Currently, the most popular anticholinergic agent used for treatment of motion sickness is the centrally acting antimuscarinic scopolamine hydrobromide (Transderm-Scop), or hyoscine, which is delivered via a cutaneous patch consisting of a drug reservoir that contains 1.5 mg of scopolamine, mineral oil, and polyisobutylene sandwiched between polyester film and an adhesive layer. The patch is applied to an area of intact skin behind the ear and delivers a continuous dose of scopolamine to the systemic circulation for 3 days. Scopolamine prevents motion-induced nausea by inhibiting vestibular input to the central nervous system (CNS), resulting in inhibition of the vomiting reflex. It may also have a direct action on the vomiting center. Although scopolamine is an atropine derivative, it differs in its central and peripheral antimuscarinic effects. As might be expected, it shares with atropine many undesirable side effects, including blurred vision resulting from dilated pupils, dry mucous membranes, and other problems denoted by the well-known mnemonic, "hot as hell, dry as a bone, blind as a bat, mad as a hatter." Particular care should be taken for patients who require mental alertness and those with impaired metabolic liver or kidney function, or with pyloric, urinary bladder neck, or intestinal obstruction. Scopolamine is contraindicated in patients at risk of narrow-angle glaucoma and should be discontinued immediately if ocular pain occurs. Although the drug information (10) states that blurred vision is temporary, patients have complained to me of persistent visual disturbance lasting more than 3 weeks after removal of the patch. The patch can be applied alternately behind each ear for long-term prevention of motion sickness, but discontinuation may cause withdrawal symptoms, including nausea, dizziness, headache, and equilibrium disturbance.

Antihistamines

Numerous antihistamines are available to prevent motion sickness, although it is likely that their benefit is derived from their intrinsic anticholinergic properties, rather than their antihistamine properties. Patients should be advised that antihistamines characteristically cause a variable degree of drowsiness, which is greatly exacerbated by alcohol and other sedatives.

The most popular of these agents is meclizine hydrochloride, a histamine-receptor blocker that presumably prevents motion sickness by blocking muscarinic receptors in the CNS. Meclizine is contraindicated in patients with respiratory difficulties (eg, emphysema, chronic bronchitis), glaucoma, or enlarged prostate. Buclizine hydrochloride (Bucladin-S Softabs) contains tartrazine (FD&C Yellow No. 5), which may cause an allergic reaction in susceptible individuals, particularly those with aspirin hypersensitivity. Diphenhydramine hydrochloride should be used with caution in patients with a history of bronchial asthma, increased intraocular pressure, hyperthyroidism, cardiovascular disease, or hypertension. Adverse effects include sedation, somnolence, dizziness, and thickened bronchial secretions. Dimenhydrinate, a chlorotheophylline salt of diphenhydramine, is available in chewable tablet form over the counter. Cyclizine (Marezine), a piperazine that causes

less drowsiness than other antihistamines, affects the stomach directly and may be preferable to the previously mentioned antihistamines (11).

Physicians may encounter foreign travelers who use cinnarizine (Stugeron), which is widely used internationally and seems to be the drug of choice in the United Kingdom, Germany, and many other foreign countries. It has not yet been approved for use in the United States.

Trimethobenzamide hydrochloride is an antihistamine structurally, but it has weak antihistamine activity. However, its antiemetic effects are similar to those of the phenothiazines, with fewer side effects.

Sympathomimetics

Sympathomimetic drugs counteract motion sickness both individually and in a synergistic combination with anticholinergic agents. Dextroamphetamine sulfate and various formulations of ephedrine are the most effective and may be used to avoid sedation in situations where alertness is required.

Nonpharmacologic remedies

Alternative medicine remedies are becoming increasingly popular and many have been recommended for treatment of motion sickness. The most popular herbal preparation for nausea is ginger root (*Zingiber officinale*), given in candied form, powdered in capsules, or as a tea infusion. Although there is much anecdotal evidence that ginger is beneficial, a controlled trial (12) found no anti-motion sickness activity. Other herbal remedies include apricot juice, carrot juice, unroasted pumpkin or squash seeds, parsley, and peppermint tea (13). Lockie and Geddes (14) recommend numerous homeopathic remedies (eg, cocculus, ignatia, ipecac, Colchicum, nux vomica, tabacum) for nausea, and nux vomica for queasiness. The difference between these two symptoms, however, is not explained.

Acupressure has generated a great deal of interest as a nonpharmacologic means of preventing motion sickness. To control nausea and vomiting, pressure is applied to the P6 acupuncture point on the pericardial meridian, located about 3 cm from the distant palmar crease between the palmaris longus and flexor carpi radialis tendons. One study involving the popular acupressure wristband that applies pressure to this area (15) found no evidence that the band prevented motion sickness, compared with placebo. Insufficient stimulation of the P6 point was cited as a possible reason for failure. A subsequent trial (16) found that continuous vigorous manual stimulation of the P6 point was required to achieve a significant benefit.

Management

Patient characteristics (age, sex, pregnancy, lactation, concomitant illnesses, allergies, previous motion sickness) as well as the type and length of the exposure should be taken into account when prescribing motion sickness

remedies.

For short-duration exposures (eg, a "flight-seeing" tour in a small airplane), 50 to 100 mg of dimenhydrinate or 50 mg of cyclizine may be given 1 hour beforehand. For longer exposures (eg, transoceanic flights), 25 to 50 mg of meclizine, taken orally, has a duration of 24 hours. Travelers who wish to sleep through the flight may prefer to take 25 to 50 mg of diphenhydramine for its sedative effects. For extended exposures (eg, a sailing trip), transdermal scopolamine may be used. The patch should be applied at least 4 hours before the anticipated exposure. Patients should be advised of possible side effects and cautioned to wash their hands after applying the patch to avoid severe ocular symptoms, which can occur if the eye is touched with contaminated fingers. If nausea is likely to be severe, patients may benefit from 12.5 to 25 mg of promethazine or 250 mg of trimethobenzamide, given orally, rectally, intramuscularly, or intravenously.

Crew members or people whose activities require alertness may be given 25 mg of promethazine combined with 50 mg of ephedrine, or 0.6 mg of scopolamine combined with 5 to 10 mg of dextroamphetamine (the "scop-dex" combination is popular among military air crews) (6). Patients should be informed that dextroamphetamine is a controlled substance and may produce a positive result on drug screening tests. For routine use, it may be preferable to replace dextroamphetamine with ephedrine, which is not a controlled substance. The latter is somewhat less effective, however (17).

Elderly passengers tend to be more resistant to motion sickness and may not require medication. Dosages should be halved and particular care should be taken with anticholinergics if there is concern about side effects.

Pregnant women are particularly susceptible to nausea caused by motion sickness. Adequate hydration should be emphasized. Although promethazine is a Category C drug (no adequate studies in humans; risk cannot be ruled out), it was considered the agent of choice for prevention or relief of motion sickness in a review of travel medicine during pregnancy (18). Meclizine, cyclizine, diphenhydramine, and dimenhydrinate are Category B drugs (no evidence of risk in humans) and also may be safely used. Metoclopramide is effective in pregnancy, but it is a potent lactation stimulant. Buclizine and other antihistamines, as well as scopolamine, are Category C drugs that are not recommended. Ginger root is often recommended as a safe alternative during pregnancy (18). An older German government investigation of herbal medicine advised against the use of ginger during pregnancy because of reported mutagenic properties. The current report, however, states that ginger is safe in therapeutic doses and is no longer contraindicated during pregnancy (19).

Children older than 2 years of age may be given 1 to 1.5 mg/kg of dimenhydrinate 1 hour before exposure, then every 6 hours. Sedatives, such as 1 mg/kg of di-

phenhydramine given no more than once every 4 hours, may help children to sleep during a long flight, but the efficacy of these agents in improving overall travel comfort has not been proved. Trimethobenzamide capsules or suppositories may also be useful in children, but there is concern about Reye's syndrome (as with aspirin use) (20). If any of these drugs are to be given, a test dose should be attempted before the trip to ensure that the child does not have a paradoxic reaction of excitability.

Table 2 lists general recommendations for patients to prevent motion sickness.

Table 2. General advice for avoiding motion sickness

Eat a light meal no less than 3 hr before exposure
Avoid dairy products and foods high in protein, calories, or sodium before exposure
Avoid alcohol, smoking, and disagreeable odors
Increase ventilation or exposure to cool, fresh air
Avoid visual stimuli (eg, reading, watching videos)
Focus on a stable horizon or external object
Limit head movements (eg, press head into headrest)
Stay in central location on boat or in airplane
Sit in front seat of car or drive rather than be a passenger
Lie in supine position

Summary

Motion sickness is an exceedingly common disorder about which primary care physicians are likely to be consulted for advice and treatment. Appropriate management should be based on patient characteristics and the type and length of the exposure and should include general preventive recommendations and directed pharmacologic agents. Education for patients about the causes of motion sickness and how to prevent it can alleviate anxiety and enhance their enjoyment of travel and recreation.

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ATTENDEES (Continued)

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BRENDA CARR, M.D.
MARKHAM C. LUKE, M.D., Ph.D.
JOSEPH PORRES, M.D., Ph.D.
JONATHAN WILKIN, M.D.

ALSO PRESENT:

JOANNE M. FRASER, Ph.D.

C O N T E N T S

C O N T E N T S (Continued)

DR. LEYDEN: I think all of us would agree the answer is both. The primary mechanism of action is working on one of the multiple areas of pathophysiology for most drugs. Most drugs only work on one area. There's one drug that works on all of them. We call it Accutane. Most drugs only work on one area and slightly on another and basically help to prevent the formation of new lesions and also to a certain degree -- and the vehicle also to a certain degree has effects on speeding the resolution of more superficial, less inflamed lesions. So it's primarily the prevention of new lesions.

DR. STERN: Well, I'm glad I got that one right for once.

Dr. King.

DR. KING: Under the concept of beauty is in the eyes of the beholder, is the FDA going to look at the global assessment by the patient? We're talking about the operation was a success and the patient died. You can reduce comedones by a lot sometimes and we all have experience of the patient not necessarily thinking it was a great therapy. So is that somehow going to be in this discussion or not?

DR. CARR: At present the subjective evaluation is not part of what we're considering. Part of the problem with quality of life or patient perception of improvement

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Publication Date October 2001

Questions and Answers About Acne

This fact sheet contains general information about acne. It describes what acne is and how it develops, the causes of acne, and the treatment options for various forms of acne. Information is also provided on caring for the skin. If you have further questions after reading this booklet, you may wish to discuss them with your doctor.

What Is Acne?

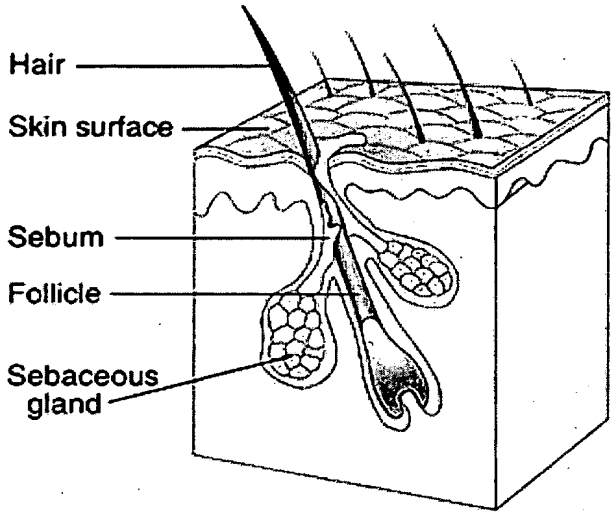
Acne is a disorder resulting from the action of hormones on the skin's oil glands (sebaceous glands), which leads to plugged pores and outbreaks of lesions commonly called pimples or zits. Acne lesions usually occur on the face, neck, back, chest, and shoulders. Nearly 17 million people in the United States have acne, making it the most common skin disease. Although acne is not a serious health threat, severe acne can lead to disfiguring, permanent scarring, which can be upsetting to people who are affected by the disorder.

How Does Acne Develop?

Doctors describe acne as a disease of the pilosebaceous units (PSUs). Found over most of the body, PSUs consist of a sebaceous gland connected to a canal, called a follicle, that contains a fine hair (see

"Normal Pilosebaceous Unit" diagram, below). These units are most numerous on the face, upper back, and chest. The sebaceous glands make an oily substance called sebum that normally empties onto the skin surface through the opening of the follicle, commonly called a pore. Cells called keratinocytes line the follicle.

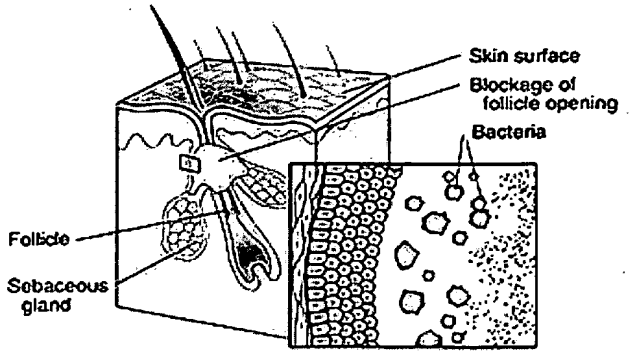
Normal Pilosebaceous Unit



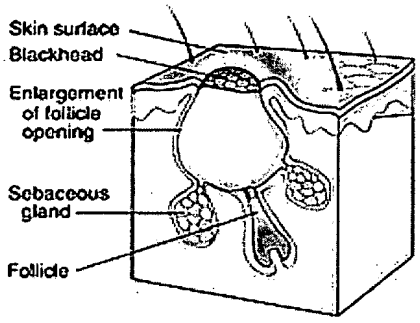
The hair, sebum, and keratinocytes that fill the narrow follicle may produce a plug, which is an early sign of acne. The plug prevents sebum from reaching the surface of the skin through a pore. The mixture of oil and cells allows bacteria *Propionibacterium acnes (P. acnes)* that normally live on the skin to grow in the plugged follicles. These bacteria produce chemicals and enzymes and attract white blood cells that cause inflammation. (Inflammation is a characteristic reaction of tissues to disease or injury and is marked by four signs: swelling, redness, heat, and pain.) When the wall of the plugged follicle breaks down, it spills everything into the nearby skin--sebum, shed skin cells, and bacteria--leading to lesions or pimples.

People with acne frequently have a variety of lesions, some of which are shown in the diagrams below. The basic acne lesion, called the comedo (KOM-e-do), is simply an enlarged and plugged hair follicle. If the plugged follicle, or comedo, stays beneath the skin, it is called a closed comedo and produces a white bump called a whitehead. A comedo that reaches the surface of the skin and opens up is called a blackhead because it looks black on the skin's surface. This black discoloration is not due to dirt. Both whiteheads and blackheads may stay in the skin for a long time.

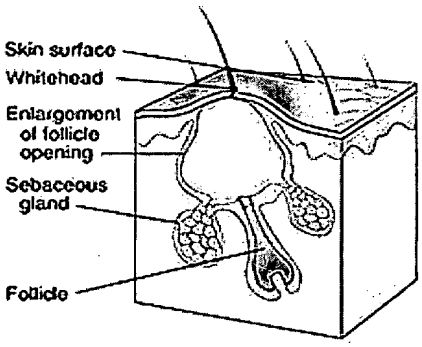
Types of Lesions



Microcomedo



Open Comedo (Blackhead)



Closed Comedo (Whitehead)

Other troublesome acne lesions can develop, including the following:

- **Papules**--inflamed lesions that usually appear as small, pink bumps on the skin and can be tender to the touch
- **Pustules (pimples)**--papules topped by pus-filled lesions that may be red at the base
- **Nodules**--large, painful, solid lesions that are lodged deep within the skin
- **Cysts**--deep, painful, pus-filled lesions that can cause scarring.

What Causes Acne?

The exact cause of acne is unknown, but doctors believe it results from

several related factors. One important factor is an increase in hormones called androgens (male sex hormones). These increase in both boys and girls during puberty and cause the sebaceous glands to enlarge and make more sebum. Hormonal changes related to pregnancy or starting or stopping birth control pills can also cause acne.

Another factor is heredity or genetics. Researchers believe that the tendency to develop acne can be inherited from parents. For example, studies have shown that many school-age boys with acne have a family history of the disorder. Certain drugs, including androgens and lithium, are known to cause acne. Greasy cosmetics may alter the cells of the follicles and make them stick together, producing a plug.

Factors That Can Make Acne Worse

Factors that can cause an acne flare include:

- Changing hormone levels in adolescent girls and adult women 2 to 7 days before their menstrual period starts
- Friction caused by leaning on or rubbing the skin
- Pressure from bike helmets, backpacks, or tight collars
- Environmental irritants, such as pollution and high humidity
- Squeezing or picking at blemishes
- Hard scrubbing of the skin.

Myths About the Causes of Acne

There are many myths about what causes acne. Chocolate and greasy foods are often blamed, but foods seem to have little effect on the development and course of acne in most people. Another common myth is that dirty skin causes acne; however, blackheads and other acne lesions are not caused by dirt. Finally, stress does not cause acne.

Who Gets Acne?

People of all races and ages get acne. It is most common in adolescents and young adults. Nearly 85 percent of people between the ages of 12 and 24 develop the disorder. For most people, acne tends to go away by the time they reach their thirties; however, some people in their forties and fifties continue to have this skin problem.

How Is Acne Treated?

Acne is often treated by dermatologists (doctors who specialize in skin problems). These doctors treat all kinds of acne, particularly severe cases. Doctors who are general or family practitioners, pediatricians, or internists may treat patients with milder cases of acne.

The goals of treatment are to heal existing lesions, stop new lesions from forming, prevent scarring, and minimize the psychological stress and embarrassment caused by this disease. Drug treatment is aimed at reducing several problems that play a part in causing acne: abnormal clumping of cells in the follicles, increased oil production, bacteria, and inflammation. Depending on the extent of the person's acne, the doctor will recommend one of several over-the-counter (OTC) medicines or prescription medicines that are topical (applied to the skin) or systemic

(taken by mouth). The doctor may suggest using more than one topical medicine or combining oral and topical medicines.

Treatment for Blackheads, Whiteheads, and Mild Inflammatory Acne

Doctors usually recommend an OTC or prescription topical medication for people with mild signs of acne. Topical medicine is applied directly to the acne lesions or to the entire area of affected skin.

Benzoyl peroxide, resorcinol, salicylic acid, and sulfur are the most common topical OTC medicines used to treat acne. Each works a little differently. Benzoyl peroxide is best at killing *P. acnes* and may reduce oil production. Resorcinol, salicylic acid, and sulfur help break down blackheads and whiteheads. Salicylic acid also helps cut down the shedding of cells lining the follicles of the oil glands. Topical OTC medications are available in many forms, such as gel, lotion, cream, soap, or pad.

In some patients, OTC acne medicines may cause side effects such as skin irritation, burning, or redness. Some people find that the side effects lessen or go away with continued use of the medicine. Severe or prolonged side effects should be reported to the doctor.

OTC topical medicines are somewhat effective in treating acne when used regularly. Patients must keep in mind that it can take 8 weeks or more before they notice their skin looks and feels better.

Treatment for Moderate to Severe Inflammatory Acne

Patients with moderate to severe inflammatory acne may be treated with prescription topical or oral medicines, alone or in combination.

Prescription Topical Medicines

Several types of prescription topical medicines are used to treat acne, including antibiotics, benzoyl peroxide, tretinoin, adapalene, and azelaic acid. Antibiotics and azelaic acid help stop or slow the growth of bacteria and reduce inflammation. Tretinoin, a type of drug called a retinoid that contains an altered form of vitamin A, is an effective topical medicine for stopping the development of new comedones. It works by unplugging existing comedones, thereby allowing other topical medicines, such as antibiotics, to enter the follicles. The doctor may also prescribe newer retinoids or retinoid-like drugs, such as tazarotene or adapalene, that help decrease comedo formation.

Like OTC topical medicines, prescription topical medicines come as creams, lotions, solutions, or gels. The doctor will consider the patient's skin type when prescribing a product. Creams and lotions provide moisture and tend to be good for people with sensitive skin. Gels and solutions are generally alcohol based and tend to dry the skin. Therefore, patients with very oily skin or those who live in hot, humid climates may prefer them. The doctor will tell the patient how to apply the medicine and how often to use it.

Some people develop side effects from using prescription topical medicines. Initially, the skin may look worse before improving. Common

side effects include stinging, burning, redness, peeling, scaling, or discoloration of the skin. With some medicines, like retinoids, these side effects usually decrease or go away after the medicine is used for a period of time. Patients should report prolonged or severe side effects to their doctor. Between 4 and 8 weeks will most likely pass before patients see their skin improve.

Prescription Oral Medicines

For patients with moderate to severe acne, the doctor often prescribes oral antibiotics (taken by mouth). Oral antibiotics are thought to help control acne by curbing the growth of bacteria and reducing inflammation. Prescription oral and topical medicines may be combined. For example, benzoyl peroxide may be combined with clindamycin, erythromycin, or sulfur. Other common antibiotics used to treat acne are tetracycline, minocycline, and doxycycline. Some people have side effects when taking these antibiotics, such as an increased tendency to sunburn, upset stomach, dizziness or lightheadedness, and changes in skin color. Tetracycline is not given to pregnant women, nor is it given to children under 8 years of age because it might discolor developing teeth. Tetracycline and minocycline may also decrease the effectiveness of birth control pills. Therefore, a backup or another form of birth control may be needed. Prolonged treatment with oral antibiotics may be necessary to achieve the desired results.

Treatment for Severe Nodular or Cystic Acne

People with nodules or cysts should be treated by a dermatologist. For patients with severe inflammatory acne that does not improve with medicines such as those described above, a doctor may prescribe isotretinoin (Accutane*), a retinoid. Isotretinoin is an oral drug that is usually taken once or twice a day with food for 15 to 20 weeks. It markedly reduces the size of the oil glands so that much less oil is produced. As a result, the growth of bacteria is decreased.

* Brand names included in this booklet are provided as examples only, and their inclusion does not mean that these products are endorsed by the National Institutes of Health or any other Government agency. Also, if a particular brand name is not mentioned, this does not mean or imply that the product is unsatisfactory.

Advantages of Isotretinoin (Accutane)

Isotretinoin is a very effective medicine that can help prevent scarring. After 15 to 20 weeks of treatment with isotretinoin, acne completely or almost completely goes away in up to 90 percent of patients. In those patients where acne recurs after a course of isotretinoin, the doctor may institute another course of the same treatment or prescribe other medicines.

Disadvantages of Isotretinoin (Accutane)

Isotretinoin can cause birth defects in the developing fetus of a pregnant woman. **It is important that women of childbearing age are not pregnant and do not get pregnant while taking this medicine.** Women must use two separate effective forms of birth control at the same time for 1 month before treatment begins, during the entire course of treatment, and for 1 full month after stopping the drug. They should ask their doctor when it is safe to get pregnant after they have stopped taking Accutane.

Some people with acne become depressed by the changes in the appearance of their skin. Changes in mental health may be intensified during treatment or soon after completing a course of medicines like Accutane. A doctor should be consulted if a person feels unusually sad or has other symptoms of depression, such as loss of appetite or trouble concentrating.

Other possible side effects include dry eyes, mouth, lips, nose, or skin; itching; nosebleeds; muscle aches; sensitivity to the sun; and, sometimes, poor night vision. More serious side effects include changes in the blood, such as an increase in triglycerides and cholesterol, or a change in liver function. To make sure Accutane is stopped if side effects occur, the doctor monitors blood studies that are done before treatment is started and periodically during treatment. Side effects usually go away after the medicine is stopped.

Treatments for Hormonally Influenced Acne in Women

Clues that help the doctor determine whether acne in an adult woman is due to an excess of androgen hormones are hirsutism (excessive growth of hair in unusual places), premenstrual acne flares, irregular menstrual cycles, and elevated blood levels of certain androgens. The doctor may prescribe one of several drugs to treat women with this type of acne. Low-dose estrogen birth control pills help suppress the androgen produced by the ovaries. Low-dose corticosteroid drugs, such as prednisone or dexamethasone, may suppress the androgen produced by the adrenal glands. Finally, the doctor may prescribe an antiandrogen drug, such as spironolactone (Aldactone). This medicine reduces excessive oil production. Side effects of antiandrogen drugs may include irregular menstruation, tender breasts, headache, and fatigue.

Other Treatments for Acne

Doctors may use other types of procedures in addition to drug therapy to treat patients with acne. For example, the doctor may remove the patient's comedones during office visits. Sometimes the doctor will inject cortisone directly into lesions to help reduce the size and pain of inflamed cysts and nodules.

Early treatment is the best way to prevent acne scars. Once scarring has occurred, the doctor may suggest a medical or surgical procedure to help reduce the scars. A superficial laser may be used to treat irregular scars. Another kind of laser allows energy to go deeper into the skin and tighten the underlying tissue and plump out depressed scars. Dermabrasion (or microdermabrasion), which is a form of "sanding down" scars, is sometimes combined with the subsurface laser treatment. Another treatment option for deep scars caused by cystic acne is the transfer of fat from one part of the body to the face.

How Should People With Acne Care for Their Skin?

Clean Skin Gently

Most doctors recommend that people with acne gently wash their skin with a mild cleanser, once in the morning and once in the evening and after heavy exercise. Some people with acne may try to stop outbreaks and oil production by scrubbing their skin and using strong detergent

soaps and rough scrub pads. However, scrubbing will not improve acne; in fact, it can make the problem worse. Patients should ask their doctor or another health professional for advice on the best type of cleanser to use. Patients should wash their face from under the jaw to the hairline. It is important that patients thoroughly rinse their skin after washing it. Astringents are not recommended unless the skin is very oily, and then they should be used only on oily spots. Doctors also recommend that patients regularly shampoo their hair. Those with oily hair may want to shampoo it every day.

Avoid Frequent Handling of the Skin

People who squeeze, pinch, or pick their blemishes risk developing scars or dark blotches. People should avoid rubbing and touching their skin lesions.

Shave Carefully

Men who shave and who have acne can test both electric and safety razors to see which is more comfortable. Men who use a safety razor should use a sharp blade and soften their beard thoroughly with soap and water before applying shaving cream. Nicking blemishes can be avoided by shaving lightly and only when necessary.

Avoid a Sunburn or Suntan

Many of the medicines used to treat acne can make a person more prone to sunburn. A sunburn that reddens the skin or suntan that darkens the skin may make blemishes less visible and make the skin feel drier. However, these benefits are only temporary, and there are known risks of excessive sun exposure, such as more rapid skin aging and a risk of developing skin cancer.

Choose Cosmetics Carefully

People being treated for acne often need to change some of the cosmetics they use. All cosmetics, such as foundation, blush, eye shadow, and moisturizers, should be oil free. Patients may find it difficult to apply foundation evenly during the first few weeks of treatment because the skin may be red or scaly, particularly with the use of topical tretinoin or benzoyl peroxide. Oily hair products may eventually spread over the forehead, causing closed comedones. Products that are labeled as noncomedogenic (do not promote the formation of closed pores) should be used; in some people, however, even these products may cause acne.

What Research Is Being Done on Acne?

Medical researchers are working on new drugs to treat acne, particularly topical antibiotics to replace some of those in current use. As with many other types of bacterial infections, doctors are finding that, over time, the bacteria that are associated with acne are becoming resistant to treatment with certain antibiotics. Research is also being conducted by industry on the potential side effects of isotretinoin and the long-term use of medicines used for treating acne.

Scientists are working on other means of treating acne. For example,

researchers are studying the biology of sebaceous cells and testing a laser in laboratory animals to treat acne by disrupting sebaceous glands. Scientists are also studying the treatment of androgenic disorders, including acne, in men by inhibiting an enzyme that changes testosterone to a more potent androgen.

Where Can People Find More Information on Acne?

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
National Institutes of Health
1 AMS Circle
Bethesda, MD 20892-3675
Phone: 301-495-4484 or 877-22-NIAMS (226-4267) (free of charge)
TTY: 301-565-2966
Fax: 301-718-6366
www.niams.nih.gov

NIAMS provides information about various forms of arthritis and rheumatic disease and bone, muscle, joint, and skin diseases. It distributes patient and professional education materials and refers people to other sources of information. Additional information and updates can also be found on the NIAMS Web site.

American Academy of Dermatology
P.O. Box 4014
Schaumburg, IL 60168-4014
Phone: 847-330-0230 or 888-462-3376 (free of charge)
Fax: 847-330-0050
www.aad.org

This national organization can provide referrals to dermatologists. It also publishes a brochure on acne for adults and a fact sheet for young people. These are available on the organization's Web site or can be obtained by calling or writing to the academy.

Acknowledgments

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The mission of the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), a part of the National Institutes of Health (NIH), is to support research into the causes, treatment, and prevention of arthritis and musculoskeletal and skin diseases, the training of basic and clinical scientists to carry out this research, and the dissemination of information on research progress in these diseases. The National Institute of Arthritis and Musculoskeletal and Skin Diseases Information Clearinghouse is a public service sponsored by the NIAMS that provides health information and information sources. Additional information can be found on the NIAMS Web site at www.niams.nih.gov.

Additional copies of this booklet are available from

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Melatonin and Jet Lag

The hormone melatonin, in conjunction with exercise and exposure to light, may help the body resynchronize sleep patterns after traveling across several time zones, according to a new study in the Journal of Pineal Research (2002;32:41-6). Melatonin, a hormone manufactured in the brain that promotes sleep, is produced in high amounts during periods of darkness. Research suggests that taking supplemental melatonin may help travelers get back to a regular sleep pattern more quickly than waiting for the body to regulate the sleep cycle on its own.

Researchers investigated the effects of 3 mg per night of supplemental melatonin on 22 professional soccer players and coaches traveling across twelve time zones. All participants engaged in moderate exercise outdoors twice a day for a total of six hours. The athletes recovered from their jet lag after approximately two days, whereas the expected time of recovery after traveling across 12 time zones is about six days. These results show that melatonin, exercise, and light exposure significantly decrease the time required to return to normal sleep patterns.

While this study examines the effect of melatonin on people traveling halfway around the world, other studies have shown that melatonin has the same beneficial effect when shorter distances were traveled. The optimal intake amount of melatonin ranges from 0.5 mg to 3 mg and is best taken 30 minutes before bedtime.

In addition to treating jet lag, melatonin may also help those suffering from insomnia and swing shift workers whose sleeping time changes from week to week. Although there is little research to support using melatonin for swing shift workers, given its safety record it would be reasonable to try.

There is emerging research suggesting melatonin may be useful in the treatment of certain types of cancer, particularly when it is taken in conjunction with specific chemotherapy protocols. However, more research is necessary to determine the usefulness of melatonin as an anti-cancer agent.

Although melatonin is generally safe, too much may produce side effects, especially a feeling of being overtired or groggy. Because of this potential side effect, it is recommended not to drive or operate machinery for several hours after taking melatonin. In addition, the long-term safety of melatonin has not been adequately studied; therefore, one should consult a physician before beginning treatment with melatonin to determine whether it is appropriate and in what amounts.

For product information click HERE

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Melatonin Is Popular, But Is It Safe?

By Andrea Pennington, M.D.

Has anyone ever suggested that you take melatonin to help get your sleep patterns back on track? Or perhaps offered it to alleviate jet lag? Despite the popularity of this hormone, which helps regulate the sleep/wake cycle, few studies prove its safety, let alone the appropriate dose.

In fact, researchers say that more studies are in order for the supplement, which works much like natural melatonin does, to help the body readjust to new time zones and promote sleep.

Why the concern over this popular dietary supplement, which is widely recommended in the media? For one, it's not regulated by the FDA, which means you can't be sure what sorts of impurities are contained in the bottle you buy — let alone how much of the active ingredient you're getting.

Especially important is the need to determine the effects of melatonin when taking other prescription drugs, including anticoagulants (blood thinners) and anti-epilepsy medications.

But because millions of people have used the supplement for several years without any health complications, I'm comfortable advising people to take the supplement as long as they don't take any prescription drugs.

While some studies show that melatonin can help prevent or lessen jet lag, the optimal dose has not been established. But a study published in December 2002 found that 0.5 mg to 5 mg of melatonin taken over a two- to five-day period was a safe and effective dose. More than 5 mg did not improve results.

If you're uncomfortable taking melatonin supplements, try the following to help prevent jeg lag and promote sleep:

- Get adequate sleep before your trip.
- Sleep the same amount of time as you do at home.
- Eat well-balanced meals and avoid overeating.
- Adopt local mealtimes and stay active during daylight hours. If you're only visiting a destination for one day, stay on your local home time.
- Exercise. Physical activity, of course, not only creates energy, it induces sleep.
- Avoid excessive amounts of alcohol.

Andrea Pennington, M.D.is the medical director for Discovery Health Online and spokesperson for Discovery Health Channel. She is co-founder and president of The Pennington Institute for Health and Wellness in Silver Spring, Md.

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Super Melatonin Plus helps relieve insomnia & reduce jet lag. This is a unique formulation combining Melatonin with natural vitamins and minerals that have been used for sleep quality and restoring inner balance. Key ingredients include vitamin B-6 and Magnesium Carbonate. Added to these nutrients are calming herbs including Valerian root, Ginger root, Chamomile and Hops. Melatonin is a naturally occurring hormone secreted by the pineal gland. Melatonin has been suggested for insomnia, jet lag, weak immune system, high cholesterol, anti-aging properties and cardiovascular health.

Product Disclaimers

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

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Documents Relating to the Prevention of Asthma and Nocturnal Asthma

Mehta
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Asthma controller drugs

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Asthma
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The Baby Page
Vaccination
Food and drink
Other problems of childhood

This article written by:
Dr. Parang Mehta
About Dr Parang
Contact Dr Parang

Can asthma be controlled at all?

Yes, it can. In fact, control is the best that we can hope for, at this time. Like diabetes and hypertension, asthma does not yet have a reliable cure.

Good medical treatment, strict avoidance measures against allergens and triggers, and strong motivation on the part of the affected child and parents are required. Given all these, control of asthma is not only possible, but is to be expected.

The controller drugs that are used currently do a rather good job of asthma control in all but a few children with severe asthma. Children on these drugs can realise the aims of asthma management -- a normal life, full participation in all childhood activities including school and sports, no school absenteeism, no emergency visits for asthma, no hospitalisations, and sleeping through the night without symptoms.

These are the drugs that control a child's asthma. Children with mild, intermittent asthma do not need any controller therapy; all children with more severe forms of asthma should be on controller therapy. This therapy is aimed at keeping the asthma under control, thus protecting the lungs from irreversible damage and allowing the child a normal life.

Since these drugs have to be taken for a long time, safety is more than ordinarily important. Acceptance by the child is also essential - the best therapy will fail if the child doesn't take it. Factors that promote acceptance are low number of daily doses, no need for doses at school, low incidence of side effects, and proper understanding of the requirement of therapy.

Sodium cromoglycate

This drug is believed to reduce the inflammation in the airways and so reduce the acute attacks of asthma. The safest of all anti asthma drugs. It is often taken by children for years, and side effects are rare. The onset of action takes some weeks, and many patients do not benefit at all. Cromoglycate is the drug of choice for initiating treatment in mild asthma.

It is also useful as pretreatment in children who suffer from exercise induced asthma. A puff of this drug, taken before participating in games, will protect the child.

Problems with the drug include dosing four times a day, and cost significantly higher than corticosteroids.

Why should asthma be controlled?

It is possible to take no long term treatment for asthma, and take reliever drugs by inhalation when needed. Some children who have mild, intermittent asthma are advised to do just this.

However, if the asthma is of severity greater than this, it means that the disease process in the lungs is also more severe. The inflammation of asthma is known to damage the lungs permanently, and reduce lung function and exercise tolerance. To prevent this inevitable reduction in lung function, it is necessary to take regular controller therapy.

It has been proved that early use of antiinflammatory drugs (inhaled steroids) prevents the loss of lung function. Though steroids are not drugs to be taken lightly, neither is asthma. Steroids cause a whole lot of side effects, but these are rare with the low doses used for inhaled therapy.

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Inhaled steroids

The mainstay of asthma control today. The steroids used for inhalation have some properties in common - they act on the surface of the airways, and they are rapidly inactivated by the liver. This latter property prevents side effects. The three drugs available in India are beclomethasone, budesonide, and fluticasone.

These drugs are reliably effective in asthma. They reduce airway inflammation and bronchial hyperresponsiveness, and prevent the deterioration in lung function that is an accompaniment of asthma. Used regularly, they can allow the child to have a normal life. At low doses, and used with precautions to reduce side effects, they have been found to be very safe at low doses. At high doses, too, they are far safer than the doses of oral steroids that would be required to maintain equivalent control of asthma.

Advantages of this class drugs is that they need to be taken only twice a day, thus eliminating any need for medication in school. They are less expensive than cromoglycate, and more effective Side effects include fungal infection of the mouth, hoarseness, and cough. At high doses, they may also cause growth reduction, and suppression of the pituitary and adrenal glands, though these effects are controversial. They may sometimes cause cataracts, and thinning of the bones.

As with all treatment, the risks of a drug must be weighed against the risks of therapy. We are used to think of asthma as a troublesome illness, but children die of asthma. Regular inhaled steroid therapy has been shown to reduce asthma deaths. Even for mildre asthma, the small risks of adverse effects are far outweighed by the benefits.

Long acting beta agonists

These drugs act on the airways to dilate them, and similar to salbutamol and terbutaline. They are slower to act, but their action persists for 8-10 hours. This makes them good drugs for those children who have symptoms at night, or who get breathless during games or physical education in school. A single dose at bedtime or before school can control these problems.

However, long acting beta agonists are not recommended for solo use in the control of asthma. They effectively relieve symptoms, giving a false sense of well being, while the asthma progresses in the lungs, sometimes to a dangerous extent.

Their recommended use is as add ons to inhaled steroid therapy. Used thus, they reduce symptoms and improve asthma control at lower levels of steroid dose. This steroid sparing effect is valuable, as it reduces the adverse effects of steroid therapy.

Slow release theophylline

Some children on inhaled steroid therapy are well controlled during the day, but have symptoms during the night. Though theophylline has fallen out of favour in the treatment of acute asthma, it is useful here. Slow release forms of theophylline maintain blood of the drug for 8-12 hours, and single dose, given at night time, will control the nocturnal symptoms, and obviate the need for a higher dose of steroid. This steroid sparing effect ...

Theophylline was earlier used to control asthma at higher doses round the clock. It had many side effects including stomach upset, poor sleep, and deteriorating school performance. The single night time dose is relatively safe.

Leukotrienne antagonists

The newest drugs in anti asthma therapy. So new, they aren't yet available in India. Zafirlukast can only be used in children above 12 years, but Montelukast can be used in children as young as 2 years. They are orally effective drugs, and may be of value in children who cannot (or will not) take inhaled therapy.

These drugs reduce airway inflammation, improve asthma control, and are especially useful for children who have exercise induced asthma. They are recommended as solo therapy only for mild asthma; for all more severe forms of asthma, they are to be used as add ons to steroids.

Oral steroids

Some children have severe asthma, with daily symptoms, a restricted lifestyle, and frequent hospitalisation, in spite

of other treatment at maximal doses. These children are candidates for oral steroid therapy. Oral steroids are very effective, but an unattractive option because of significant side effects.

Oral steroids can cause suppression of growth, suppression of the pituitary and adrenal glands, thinning of the bones, obesity, cataracts, raised blood pressure, diabetes, muscle weakness, and several other adverse effects. For this reason, oral steroid therapy requires careful monitoring by an expert, and ongoing efforts to wean the child off it as soon as possible.

The drug most commonly used is prednisolone. Giving the entire daily requirement as a single dose in the morning has been found to reduce side effects. Once control is achieved, it may be possible to switch to an alternate day schedule.

Measures to reduce the dose of oral steroid include concomitant inhaled steroids, and avoidance of dust and other trigger factors.

Ketotifen

This drug was introduced some years ago as an oral drug that controlled asthma. Doesn't.

Last revision: January 31, 2004

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Nocturnal Asthma

Asthma is a chronic condition in which the airways are hyperreactive (very sensitive) to certain irritants that cause them to constrict, thus making breathing difficult. This constriction (called bronchospasm) is accompanied by inflammation in the membranes lining the walls of the airways and excess production of mucus (phlegm).

The net effect has been described as a feeling that one is "breathing through a straw." Triggering irritants may include allergens, smoke, fumes and dry, cold air. Exertion during exercise or even from laughing can also cause the airways to constrict. Asthmatics vary considerably in the severity of symptoms, response to treatment and the impact of illness on their lives.

Nightime Worsening

Asthma symptoms can change a great deal during sleep. And although sleep-related asthma can occur at any time of the day, it is generally called "nocturnal asthma" since most people sleep at night. Nocturnal asthma is defined as any sleep-related worsening of reversible airway disease. Symptoms generally include shortness of breath or coughing and wheezing at night. Approximately 80 percent of severe asthmatic attacks occur between midnight and 8 a.m.

The Chronobiology of Asthma

Many biological processes occur cyclically. Chronobiology is the study of biological processes with time-related rhythms. While some biological rhythms occur monthly or annually, asthma changes fairly predictably on a 24 hour or circadian cycle.

Lung function differs even in normal, non-asthmatics between day and night. Optimal lung function
occurs about 4 p.m. and poorest about 4 a.m. In non- asthmatics, the difference is so insignificant that it goes unnoticed. But in asthmatics, lung function can change as much as 50 percent over the course of a day. Bronchial reactivity generally follows the same circadian cycle in asthmatics-greatest reactivity corresponds with poorest lung function at 4 a.m. and lowest reactivity corresponds with optimal lung function at 4 p.m.

Changes in lung function at night are likely not due to the effects of lying down. Studies show that lung function is related primarily to the time of day or night a person sleeps. Thus, the rhythms are likely to be reversed in someone who works nights and sleeps days.

Causes of Nocturnal Asthma

Nocturnal asthma is probably attributable to multiple, interactive factors rather than to a

single cause. Allergens are a major factor triggering asthma attacks. Daytime exposure to allergens can be every bit as important as exposure to allergens in the bedroom during sleep. Allergens in the airways precipitate a series of physiological events as long as three to eight hours after the initial exposure. This is called late-asthma response (LAR); it may correspond to the nighttime for some people and it can recur over several nights. Allergen exposure in the evening increases a susceptible patient's risk of LAR from 40 to 90 percent.

Asthma is an inflammatory disease. In certain people, this inflammation worsens at night and tends to correspond with circadian changes in peak expiratory flow rates (the ability to exhale rapidly). Airway secretions may be a contributing factor to nocturnal asthma. About 70 percent of asthmatics experience chronic sinusitis and/or postnasal drip. When the sinuses are cleared, daytime and nighttime symptoms of asthma often improve.

Airway temperature also influences onset of symptoms. Even a brief exposure to cold, dry air can
produce bronchospasm. The effect can be reversed by breathing warm, humidified air. Asthmatics may experience sleep apnea, characterized by brief, repetitive cessation of breathing during sleep. Resulting from an upper airway disturbance, sleep apnea triggers asthma of the lower airways.

Gastroesophageal reflux (GER) is a condition in which gastric acid "backs up" (refluxes) into the
esophagus, resulting in "heartburn." GER is caused by a faulty valve that permits the reflux of stomach contents. A variation of this condition may trigger nocturnal asthma. When a person with a faulty valve lies flat, gravity may allow for a small amount of acid to reflux far enough to be inhaled into the airway, triggering bronchospasm.

Certain hormones and other body chemicals are involved in the relaxation of smooth muscle and the cellular response leading to asthma. Circadian changes in these chemicals correlate with noted changes in lung function, but the significance of these changes is currently unclear.

Diagnosis of Nocturnal Asthma

It is important to inform your clinician if asthma symptoms worsen at night. You may be asked to monitor your lung function using a peak flow meter. This is a portable device that measures the lung volume and how quickly air can be expelled from the lungs. Decreasing values measured by the peak flow meter indicate a tightening of the airways, and can serve as an early warning of impending respiratory symptoms, such as shortness of breath and wheezing. Nocturnal asthma can be documented by recording peak flow rates at bedtime, during any awakening at night and in the morning. The readings provide an objective basis for treatment; swings in peak flow rates help indicate persons at-risk of respiratory arrest, which occurs mostly at night.

Treatment

An understanding of the circadian rhythms of asthma and the effects of various medications enables your clinician to apply the concepts of chronopharmacology- the science of precisely timed drug administration. The primary principle is to apply the most intense therapy when the disease worsens.

An inhalant drug called Serevent, (salmeterol) provides sustained effectiveness against bronchoconstriction and is therefore the treatment of choice for prevention of nocturnal asthma attacks. Anti-inflammatory inhalants may also be useful.

Corticosteroid medications are potent anti-inflammatories that are occasionally used in cases of severe asthma. Inhaled steroids are preferable to oral steroids because they present fewer side effects. However, severe nocturnal asthma may indicate the use of oral steroid medication in the evening.

Treatments that improve sinusitis, if present, can also improve nocturnal asthma. Nasal irrigation, oral decongestants and nasal steroids can reduce or eliminate upper airway inflammation and the
consequent bronchoconstriction.

If sleep apnea is present, the clinician may suggest a variety of interventions, including a change in
sleeping position, medications or a mechanical device that keeps the back of the throat open to prevent apnea. This device is called a nasal CPAP (Continuous Positive Airway Pressure). Asthmatics who experience gastroesophageal reflux (GER) are advised to raise their upper body so they sleep at a 458 angle. This prevents gravity from permitting acid reflux. Your clinician may also prescribe certain medications for GER.

If you experience signs of nocturnal asthma, be sure to inform your clinician. Remember that asthma is a reversible disease that can be managed well with proper medical supervision.

WHAT ARE THE SPECIFIC DRUGS USED TO PREVENT ASTHMA ATTACKS AND REDUCE AIRWAY INFLAMMATION?

Corticosteroids

Corticosteroids, also called glucocorticoids or steroids, are powerful anti-inflammatory drugs. Steroids are not bronchodilators (that is, they do not relax the airways) and have little effect on symptoms. Instead, they work over time to reduce inflammation and prevent permanent injury in the lungs. Many studies have now shown th the use of inhaled corticosteroids in patients with moderate to severe asthma significantly reduce the rate of rehospitalizations and deaths from asthma. Nevertheless, they are still significantly underprescribed in the patients who need them most.

Inhaled Corticosteroids. Inhalation of corticosteroids makes it possible to provide effective local anti-inflammatory activity in the lungs with minimal systemic effects. (Oral steroids have considerable side effects. They are currently recommended as the primary therapy under the following circumstances:

- For any asthmatic condition more serious than occasional episodes of mild asthma. (Low-doses of inhaled steroids may even be safe and effective for some people with mild asthma, particularly those w find themselves using beta2-agonists daily.)
- When treatment with bronchodilators is not effective.

Examples of inhaled corticosteroids are the following:

- The most recent generation of inhaled steroids include (in order of potency) fluticasone (Flovent), budesonide (Pulmicort), triamcinolone (Azmacort and others), and flunisolide (AeroBid). In general, the newer agents, are more powerful than the older generation of inhaled agents. Experts have some concern, then, that these potent agents, particularly fluticasone, may produce major side effects similar oral agents. Studies are now suggesting, however, that the same benefits can be achieved with low doses of fluticasone as with high doses, thus reducing risks for serious side effects. (Of note, budesoni appears to be safe during pregnancy.)
- The older corticosteroid inhalants are beclomethasone (Beclovent, Vanceril) and dexamethasone (Decadron Phosphate Respihaler and others). They are less powerful than the newer steroids when delivered with standard inhalers. New inhaler systems for, however, such as QVAR, which uses extra f formulations of beclomethasone to allow deep delivery into the lungs may prove to be as effective as th newer, more potent steroids.
- Inhalers that combine both long-acting beta2-agonists and corticosteroids are now available. [*See* Combinations of Corticosteroids and Long-Acting Beta2 Agonists.]

Inhaled corticosteroids must be taken regularly. It may take a month to perceive their effects and up to a year to achieve full benefits. Some of these agents may have some immediate benefits; in one study, inhaled budesonide reduced inflammation in the airways within six hours.

Optimal timing of the dose is important and may vary depending on the medication. Most of the newer inhaled steroids and even some older ones are now available as a single daily dose, which some patien may respond to.

Side effects of inhaled steroids are the following:

- The most common side effects are throat irritation, hoarseness, and dry mouth. These effects can be minimized or prevented by using a spacer device and rinsing the mouth after each treatment.
- Rashes, wheezing, facial swelling (edema), fungal infections (thrush) in the mouth and throat, and bruising are also possible but are not common with inhalators.

Inhaled steroids are generally considered safe and effective and only rarely cause any of the more serio side effects reported with prolonged use of oral steroids. A 2001 study, however, reported a higher risk f cataracts in patients over age 40. (No higher risk was observed in younger people.) Others are reporting higher risk for bone loss in patients who take inhaled steroids regularly. (A number of bone-preserving medications are now available that might safely offset this effect.) There is also some concern that the more potent agents, particularly fluticasone, suppress the adrenal system (which secretes natural steroi to a greater degree than other steroid inhalants. (This is a serious side effect of oral steroids.)

Of note, during pregnancy, inhaled budesonide and beclomethasone are considered to be generally saf

Oral Corticosteroid s. Oral agents are usually the last drugs to be added to an asthma treatment prograr and the first to be removed. Common oral corticosteroids include prednisone, prednisolone, methylprednisolone, and hydrocortisone. They very effectively reduce inflammation but are generally us only after hospitalization for an acute attack. In some severe cases, they may be used as maintenance.

- effects of prolonged use of oral steroids include cataracts, glaucoma, osteoporosis, diabetes, fluid retention, susceptibility to infections, weight gain, hypertension, capillary fragility, acne, excess hair growth, wasting of the muscles, menstrual irregularities, irritability, insomnia, and psychosis. Osteoporosis is a common and particularly severe long-term side effect of prolonged steroid use. Medications that can prevent osteoporosis include calcium supplements, parathyroid hormone, bisphosophonates, or hormone replacement therapy in post-menopausal women. Vitamin C and E ma help reduce the risk of cataracts.

Long-term use of oral steroid medications suppresses secretion of natural steroid hormones by the adrenal glands. After withdrawal from these drugs, this so-called adrenal suppression persists and it car take the body a while (sometimes up to a year) to regain its ability to produce natural steroids again. It should be noted that there have been a few cases of severe adrenal insufficiency that occurred when switching from oral to inhaled steroids, which, in rare cases, has resulted in death.

No one should stop taking any steroids without consulting a physician first, and if steroids are withdrawn regular follow-up monitoring is necessary. Patients should discuss with their physician measures for preventing adrenal insufficiency during withdrawal, particularly during stressful times, when the risk increases.

Long-Acting Beta2-Agonists and Corticosteroid Combinations

Long-acting beta2-agonists, including salmeterol (Serevent) and formoterol (Foradil), are used for preventing asthma attack (not for treating symptoms). The effects of one dose of a long-acting beta2 agonist last for abo 12 hours, so they are particularly effective during the night. These agents also may be used for prevention of exercise-induced asthma in people and to protect against aspirin-induced asthma.

As with short-acting beta2-agonists, the long-acting forms have no effect on inflammation, and they should no be used alone on any regular on basis. Evidence suggests that such use may reduce the effectiveness of the short-acting beta2 agonists, which are the mainstays for treating acute attacks. In patients with moderate to severe asthma, the long-acting beta2 agonists are best used in combination with anti-inflammatory drugs. Adding these agents to a steroid regimen, in fact, may help prevent the need for higher doses of steroids. Sin devices that contain both agents are now available in the US (Advair) and parts of Europe (Seretide, Symbico These inhalers appear to be safe and possibly more effective than either agent used alone for patients who d not respond well to other agents.

Warning on Salmeterol. Both salmeterol and formoterol are beneficial and improve the quality of life. Formote has a much faster action than salmeterol and may achieve better control of nighttime asthma. Formoterol, in fact, works almost as fast as the short-acting albuterol and is sometimes used to treat asthma symptoms. Salmeterol, however, requires up to 20 minutes to achieve effectiveness and should never be used for stoppi an attack. There is a danger then of overdose if a patient is not aware of this delay and takes additional dose

achieve faster relief. (Overdose has been fatal in rare cases.) The risk appears to be highest in elderly patient with severe asthma. People using long-acting beta2 agonists should take the following precautions:

- The medication should *not* be stored in locations that are easily accessible during acute attacks, such a by the bed or in a pocketbook.
- Salmeterol should never be used for treatment of acute episodes; for this purpose, short-acting bronchodilators should be used. (Formoterol has a faster action and may, in some cases, be used for treating symptoms, but patients should check with their physician.)

Side Effects. Side effects of long-acting beta2 agonists are similar to the short-acting agents. [S *ee* Shor Acting Beta2 Agonists *under* What Are the Specific Drugs Used to Treat Symptoms of Acute Asthma Attacks?]

Cromolyn and Similar Drugs

Cromolyn sodium (Intal) serves as both an anti-inflammatory drug and has antihistamine properties that block asthma triggers such as allergens, cold, or exercise. Nedocromil (Tilade) is similar to cromolyn. A cromolyn nasal spray called Nasalcrom has been approved for over-the-counter purchase, but only to relieve nasal congestion caused by allergies. Asthmatic patients should not use it for self-medication without the advice of a physician.

Candidates. Cromolyn is often used in children with allergic asthma, but it has also been an important treatme for exercise-induced asthma (EIA) in all age groups, for pregnant women, and possibly for preventing allergic asthma in adults as well as children. Both cromolyn and nedocromil appear to be useful for patients with aspir induced asthma. These agents do not effectively treat asthma once an attack is underway. They also have ve little long-term benefits on lung function compared to inhaled corticosteroids.

Side Effects. Side effects of cromolyn include nasal congestion, coughing, sneezing, wheezing, nausea, nosebleeds, and dry throat. Nedocromil has an unpleasant taste and some people have complained of nause headache, and spasms in the airways, but no serious side effects have been reported.

Leukotriene-Antagonists

Leukotriene-antagonists are oral medications that block leukotrienes, powerful immune system factors that, in excess, produce a battery of damaging chemicals that can cause inflammation and spasms in the airways of people with asthma. As with other anti-inflammatory agents, leukotrienes are used for prevention and not for treating acute asthma attacks.

The leukotriene-antagonists include zafirlukast (Accolate), montelukast (Singulair), zileuton (Ziflo), and pranlukast (Ultair, Onon). These agents are proving to be effective for long-term prevention of asthma, and possibly for exercise-induced asthma or aspirin-induced asthma. They may also reduce the severity of allergy symptoms, regardless of whether or not asthma is also present.

Many studies to date, however, are not finding any advantages compared to the more potent inhaled corticosteroids. Their anti-inflammatory actions are different from those of steroids, and a combination of the t agents is proving to be particularly effective, although it is not yet clear when such combinations would be useful.

Side Effects and Complications. Gastrointestinal distress is the most common side effect of leukotriene-antagonists. Very few other side effects have been reported. In general, these agents appear to be safe and well tolerated.

Of some concern are reports of Churg-Strauss syndrome in a few people taking zafirlukast or montelukast. Churg-Strauss syndrome is very rare, but it causes blood vessel inflammation in the lungs and can be life threatening. Oral steroids quickly resolve the problem. In fact, usually the syndrome has occurred in patients

who were tapering off steroids and changing over to the leukotrienes-antagonists. Some experts believe that, such cases, the steroids may simply have masked the presence of the disorder, which then developed when t steroid drugs were withdrawn. Symptoms include severe sinusitis, flu-like symptoms, rash, and numbness in t hands and feet.

Other concerns are indications of liver injury in patients taking zileuton and zafirlukast when taken at higher th standard doses. No adverse effects on the liver have been reported to date with montelukast.

WHAT ARE THE SPECIFIC DRUGS USED TO PREVENT ASTHMA ATTACKS AND REDUCE AIRWAY INFLAMMATION?

Cromolyn and Similar Drugs

Cromolyn sodium (Intal) serves as both an anti-inflammatory drug and has antihistamine properties that block asthma triggers such as allergens, cold, or exercise. Because of its proven safety record, cromolyn has been the anti-inflammatory agent of choice for prevention of asthma attacks in children over four with chronic moderate asthma. It is not a corticosteroid, so does not inhibit growth in children. Studies indicate that it also may reduce hospitalization rates almost as well as corticosteroids do, and that up to 70% of children who need asthma maintenance therapy would do well on cromolyn. (It may not provide any real benefit for children under four.)

A cromolyn nasal spray called Nasalcrom has been approved for over-the-counter purchase, but only to relieve nasal congestion caused by allergies. Asthmatic patients should not use it for self-medication without the advice of a physician. Nedocromil (Tilade) is similar to cromolyn and also prevents asthmatic reactions to cold and exercise. Ketotifen, a similar drug, may be useful in preventing allergic asthma, but may not be as effective as cromolyn.

Side Effects. Side effects of cromolyn include nasal congestion, coughing, sneezing, wheezing, nausea, nosebleeds, and dry throat. Nedocromil has an unpleasant taste and some people have complained of nausea, headache, and spasms in the airways, but no serious side effects have been reported.

Corticosteroids

Corticosteroids, also called glucocorticoids or steroids, are powerful anti-inflammatory drugs. Steroids are not bronchodilators (that is, they do not relax the airways) and have little effect on symptoms. Instead, they work over time to reduce inflammation and prevent permanent injury in the lungs. Many studies have now shown that the use of inhaled corticosteroids in patients with moderate to severe asthma significantly reduce the rate of rehospitalizations and deaths from asthma. Nevertheless, they are still significantly underprescribed in the patients who need them most.

Inhaled Corticosteroids. Inhalation of corticosteroids makes it possible to provide effective local anti-inflammatory activity in the lungs with minimal systemic effects. (Oral steroids have considerable side effects.) They are currently recommended as the primary therapy under the following circumstances:

- For any asthmatic condition more serious than occasional episodes of mild asthma. (Low-doses of inhaled steroids may even be safe and effective for some people with mild asthma, particularly those who find themselves using beta2-agonists daily.)

- When treatment with bronchodilators is not effective.

Examples of inhaled corticosteroids are the following (not all are available to children):

- The most recent generation of inhaled steroids include (in order of potency) fluticasone (Flovent), budesonide (Pulmicort), triamcinolone (Azmacort and others), and flunisolide (AeroBid). In general, the newer agents, are more powerful than the older generation of inhaled agents. Experts have some concern, then, that these potent agents, particularly fluticasone, may produce major side effects similar to oral agents. Studies are now suggesting, however, that the same benefits can be achieved with low doses of fluticasone as with high ones, thus reducing risks for serious side effects. (Of note, budesonide appears to be safe during pregnancy.)

- The older corticosteroid inhalants are beclomethasone (Beclovent, Vanceril) and dexamethasone (Decadron Phosphate Respihaler and others). They are less powerful than the newer steroids when delivered with standard inhalers. New inhaler systems for, however, such as QVAR, which uses extra fine formulations of beclomethasone to allow deep delivery into the lungs may prove to be as effective as the newer, more potent steroids.

- Budesonide (Pulmicort Respules) is available in a jet nebulizer for children from 12 months to 8 years. It is, in fact, the first such medication to be approved for children in this age group.

- Inhalers that combine both long-acting beta2-agonists and corticosteroids are now available. [*See* Combinations of Corticosteroids and Long-Acting Beta2 Agonists.]

Evidence strongly suggests that early treatment is important for children with severe asthma to prevent deterioration in lung function. In addition, a major 2000 study reported that inhaled steroids may be beneficial and safe even for children with mild to moderate asthma. In the study, inhaled budesonide was more effective than nedocromil in controlling asthma and any effect on growth was slight and temporary.

Unfortunately an estimated 10% of children do not respond to inhaled steroids, and one 1998 study has

reported that as many as 25% of adolescents may be insensitive to the drug. Of some promise is a report that the added use of intravenous immunoglobulin may be effective in such patients and reduce the need for steroids.

Side effects of inhaled steroids are the following:

- The most common side effects are throat irritation, hoarseness, and dry mouth. These effects can be minimized or prevented by using a spacer device and rinsing the mouth after each treatment.
- Rashes, wheezing, facial swelling (edema), fungal infections (thrush) in the mouth and throat, and bruising are also possible but are not common with inhalators.
- Some children experience changes in mood, memory, and behavior, but they are not permanent.
- Some studies have suggested a higher risk for gum inflammation.
- It is well known that oral steroids reduce bone density and much research has focused on the effects of inhaled steroids on growth in children. Of some comfort are two major 2000 studies confirming previous ones that reported only a slight (about half an inch) and temporary effect on children's growth. It is not yet known, however, whether inhaled steroids effect lung growth in very young children. Steroids administered using nebulizers are of particular concern. At this time, then, experts caution against them for infants and toddlers with mild asthma and urge close monitoring especially for children under five with severe asthma who are receiving high doses. Calcium supplements appear to help prevent bone loss due to inhaled steroids.
- There is also some concern that the more potent agents, particularly fluticasone, suppress the adrenal system (which secretes natural steroids) to a greater degree than other steroid inhalants. (This is a serious side effect of oral steroids.)

Oral Corticosteroid s. Oral agents are usually the last drugs to be added to an asthma treatment program and the first to be removed. Common oral corticosteroids include prednisone/prednisolone, dexamethasone, methylprednisolone, and hydrocortisone. They reduce inflammation very effectively, but children generally take them only for five days after hospitalization for an acute attack. Compliance among children can be low, however, since these agents have a bitter taste and can cause vomiting. Taking oral dexamethasone for two days may be as effective and more tolerable than the

standard a five-day regimen of prednisone/prednisolone. Prolonged use of oral steroids has widespread effects, and so they are not generally give to children for longer than a few days.

Long-Acting Beta2-Agonists and Corticosteroid Combinations

Long-acting beta2-agonists, including salmeterol (Serevent) and formoterol (Foradil), are used for preventing an asthma attack (not for treating symptoms). The effects of one dose of a long-acting beta2 agonist last for about 12 hours, so they are particularly effective during the night. These agents also may be used for prevention of exercise-induced asthma in people and to protect against aspirin-induced asthma.

As with short-acting beta2-agonists, the long-acting forms have no effect on inflammation, and they should not be used alone on any regular on basis. Evidence suggests that such use may reduce the effectiveness of the short-acting beta2 agonists, which are the mainstays for treating acute attacks. In patients with moderate to severe asthma, the long-acting beta2 agonists are best used in combination with anti-inflammatory drugs. Adding these agents to a steroid regimen, in fact, may help prevent the need for higher doses of steroids.

The long-acting drugs used most are salmeterol (Serevent) and formoterol (Foradil). In comparison studies, they appear to be equally beneficial, although Formoterol has a much faster action and may achieve better control of nighttime asthma. Formoterol, in fact, works almost as fast as the short-acting albuterol and is sometimes used to treat asthma symptoms. Studies indicate that these are safe for children and may, in fact, be particularly effective for them. In one year-long study of children with mild to moderate asthma, salmeterol was not as effective as the corticosteroid beclomethasone, but it did reduce asthma symptoms without retarding growth.

A single inhaler (Advair Diskus) that combines both long-acting beta2-agonists and corticosteroids is now available for children over age 12. This inhaler appears to be safe and possibly more effective that either agent used alone for patients who do not respond well to other treatments.

Side Effects. Side effects of long-acting beta2 agonists are similar to the short-acting agents. [S *ee* Short-Acting Beta2 Agonists *under* What Are the Specific Drugs Used to Treat Symptoms of Acute Asthma Attacks?]

Leukotriene-Antagonists

Leukotriene-antagonists are oral medications that block leukotrienes, powerful immune system factors that, in excess, produce a battery of damaging chemicals that

can cause inflammation and spasms in the airways of people with asthma. As with other anti-inflammatory agents, leukotrienes are not used for treating acute asthma attacks.

The leukotriene-antagonists include zafirlukast (Accolate), montelukast (Singulair), zileuton (Ziflo), and pranlukast (Ultair, Onon). These agents are proving to be effective for long-term prevention of asthma, including exercise-induced asthma and aspirin (or NSAID)-induced asthma. Many studies to date, however, are not finding any advantages compared to the more potent inhaled corticosteroids. Their anti-inflammatory actions are different from those of steroids, and a combination of the two agents is proving to be particularly effective, although it is not yet clear when such combinations would be useful.

Nevertheless, studies suggest that montelukast, which comes in a chewable tablet, may be particularly useful for managing asthma in small children (ages two to five) with asthma, since they have trouble with inhaled steroids. As suggested by another 2000 study on the effects of zafirlukast, they may also reduce the severity of cat allergies, regardless of whether or not asthma is also present.

Side Effects and Complications. Gastrointestinal distress is the most common side effect of leukotriene-antagonists. Very few other side effects have been reported. In general, these agents appear to be safe and well tolerated.

Of some concern are reports of Churg-Strauss syndrome in a few people taking zafirlukast or montelukast. Churg-Strauss syndrome is very rare, but it causes blood vessel inflammation in the lungs and can be life threatening. Oral steroids quickly resolve the problem. In fact, usually the syndrome has occurred in patients who were tapering off steroids and changing over to the leukotrienes-antagonists. Some experts believe that, in such cases, the steroids may simply have masked the presence of the disorder, which then developed when the steroid drugs were withdrawn. Symptoms include severe sinusitis, flu-like symptoms, rash, and numbness in the hands and feet.

Other concerns are indications of liver injury in patients taking zileuton and zafirlukast when taken at higher than standard doses. No adverse effects on the liver have been reported to date with montelukast.

Contraception. 1984 May;29(5):479-91.

Related Articles, Links

Phenoxybenzamine--an effective male contraceptive pill.

Homonnai ZT, Shilon M, Paz GF.

Phenoxybenzamine (PBZ), administered in doses up to 20 mg/day, caused aspermia following male orgasm. This led to the development of a male contraceptive pill, PBZ being the active drug. It has been shown that small doses of the drug do not change the hormonal balance of the body, nor do they affect blood pressure. In 2 to 3 days, PBZ blocks ejaculation; this is fully reversed with the cessation of treatment. The drug does not affect semen quality (testicular function), even after a long period of medication. During treatment, the vas deferens, the ampulla and the ejaculatory ducts are probably paralyzed. Cessation of medication brought full recovery of these effects and the reappearance of normal ejaculation. Men complaining of premature ejaculation reported marked improvement in their sexual performance. The recommended regimen for administering PBZ as a male contraceptive is discussed.

PMID: 6430643 [PubMed]

Hormone-Derived Oral Contraceptives. Researchers are currently at work on hormonal contraceptives that reduce levels of sperm. Some examples include the following:

- In a very small study of eight men, the oral steroids cyproterone acetate and testosterone undecanoate significantly suppressed sperm production without any major side effects. The sperm reduction was still not sufficient to completely prevent pregnancy, but adjusting the dosage may improve results. Sexual behavior was not affected.

- The hormone desogestrel is being tested. Desogestrel is a progestin, a hormone used in female contraceptives. In one study, men took this drug and were also given testosterone implants to maintain male hormones. The regimen was successful in suppressing sperm production while maintaining normal male hormone levels. Sperm production returned to normal when the men stopped taking the drug.

Hormonal contraception for men is more complicated than for women, however, since it requires add-back therapies of male hormones. There is also a typical delay of two to three months before infertility is achieved.

Gossypol. Gossypol is a chemical extracted from cotton roots. It has been used in China as a male contraceptive, and cotton root was used as folk medicine in the American South to treat menstrual pain and to induce abortions. The chemical destroys the lining of tubules in the testicles where sperm are produced, thereby inhibiting their formation. A 2000 Brazilian study reported that a male oral contraceptive derived from gossypol suppressed sperm production within up to 16 weeks. In men who were taking lower doses, sperm production returned in most of them within a year after they stopped taking the contraceptive. In the high dose group, sperm count reversed in less than half. Gossypol did not appear to reduce sexual desire or frequency of intercourse. It also may not be very effective, since even if small numbers of sperm survive, they may get through to penetrate the egg. Researchers are investigating gossypol-derived compounds that may have less toxicity. (No one should take any so-called natural gossypol product without consultation with a physician. [*See* Warning Box.])

NewScientist.com

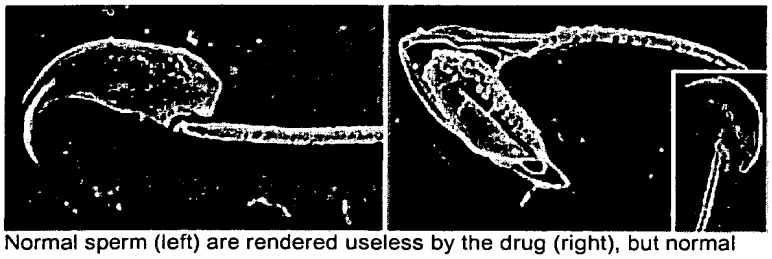
Reversible male contraceptive deforms sperm

00:01 10 December 02

NewScientist.com news service

A male contraceptive that works by deforming sperm could available within just a few years, if tests on men go well. This fast track development is possible because the drug is already licensed for use in treating a rare genetic disorder in people, called Gaucher's disease.

The drug is taken as a pill, not injected, and it could have fewer side effects than experimental hormonal male contraceptives, which include a cocktail of hormones designed to suppress sperm production while maintaining normal testosterone levels.



Normal sperm (left) are rendered useless by the drug (right), but normal sperm return when the drug is stopped (inset)

Furthermore, its contraceptive effects may be more completely reversible than other non-hormonal drugs in development, say the researchers conducting the experiments at the University of Oxford, UK.

In tests on mice, low doses of the drug interfered with the metabolism of sugar-fat compounds essential for sperm production. Sperm from the treated mice showed a range of defects, including tails that were coiled around the sperm head and abnormally shaped nuclei. Every mouse in the study was rendered infertile, and there were no obvious side effects.

"I'm excited by the potential of the new compound," says Richard Sharpe of the MRC Human Reproductive Sciences Unit at the University of Edinburgh, Scotland. But he warns that many promising male contraceptives that have shown similar results in animal models in the past have fallen by the wayside.

Usually, this has been because of problems relating to side-effects or irreversibility in people, or because a drug that has worked well in mice has not been successful when tried in men.

40 days, 40 nights

The drug, N-butyldeoxynojirimycin (NB-DNJ), inhibits an enzyme that produces glucosylceramide. This sugar-fat compound is vital for sperm creation.

In mice, sperm live no longer than three weeks before being replaced. After three weeks on the drug, the mouse in the study became fully infertile. After three weeks off, they regained their fertility. In men, the on-off period would be about 40 days, says Oxford University's Frances Platt, who led the new work.

Men would probably have to take a pill every day, she says. But she believes there would be a demand for such a drug. "People innately believe that men are not reliable individuals when it comes to contraception," she told **New Scientist**. "But different people have different requirements, and this may offer an alternative."

Sharpe agrees that there is a "huge unmet need" for alternatives to condoms or a vasectomy. "What is most appealing about these new findings is that the same or related compounds are already in clinical use, so we can be assured that no major adverse side effects have been seen," he says.

Journal reference: *Proceedings of the National Academy of Sciences* (DOI: 10.1073/pnas.262586099)

Emma Young

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Documents Relating to Female Contraception

FDA Consumer magazine
April 1997 Issue

This article originally appeared in the April 1997 *FDA Consumer* and contains revisions made in August 2002 and December 2003.

Birth Control Guide

[This information is also available in a handy chart format (22K PDF)]

Updated December 2003

The Food and Drug Administration has approved a number of birth control methods. The choice of birth control depends on factors such as a person's health, frequency of sexual activity, number of sexual partners, and desire to have children in the future. Failure rates, based on statistical estimates, are another key factor. The most effective way to avoid both pregnancy and sexually transmitted disease is to practice total abstinence (refrain from sexual contact).

Failure Rates in this chart are based on information from clinical trials submitted to the FDA during product reviews. This number represents the percentage of women who become pregnant during the first year of use of a birth control method. For methods that the FDA does not review, such as periodic abstinence, numbers are estimated from published literature. For comparison, about 85 out of 100 sexually active women who wish to become pregnant would be expected to become pregnant in a year.

Serious medical risks from contraceptives, such as stroke related to oral contraceptives, are relatively rare. This chart is a summary of important information, including risks, about drugs and devices approved by the FDA for contraception and sterilization. It is not intended to be used alone, and a health professional should be consulted regarding any contraceptive choice. Review product labeling carefully for more information on use of these products.

Male Condom, Latex/Polyurethane

FDA Approval Date: Latex: Use started before premarket approval was required. Polyurethane: cleared in 1989; available starting 1995.
Description: A sheath placed over the erect penis blocking the passage of sperm.
Failure Rate (number of pregnancies expected per 100 women per year): 11 (a, b)
Some Risks: Irritation and allergic reactions (less likely with polyurethane)
Protection from Sexually Transmitted Diseases (STDs): Except for abstinence, latex condoms are the best protection against STDs, including gonorrhea and AIDS.
Convenience: Applied immediately before intercourse; used only once and discarded. Polyurethane condoms are available for those with latex sensitivity.
Availability: Nonprescription

Female Condom

FDA Approval Date: 1993
Description: A lubricated polyurethane sheath shaped similarly to the male condom. The closed end has a flexible ring that is inserted into the vagina.
Failure Rate (number of pregnancies expected per 100 women per year): 21
Some Risks: Irritation and allergic reactions
Protection from Sexually Transmitted Diseases (STDs): May give some STD protection; not as effective as latex condom
Convenience: Applied immediately before intercourse; used only once and discarded.
Availability: Nonprescription

Diaphragm with Spermicide

FDA Approval Date: Use started before premarket approval was required.
Description: A dome-shaped rubber disk with a flexible rim that covers the cervix so that sperm cannot reach the uterus. A spermicide is applied to the diaphragm before insertion.
Failure Rate (number of pregnancies expected per 100 women per year): 17 (b, d, e)
Some Risks: Irritation and allergic reactions, urinary tract infection. (c) Risk of toxic shock syndrome, a rare but serious infection, when kept in place longer than recommended.
Protection from Sexually Transmitted Diseases (STDs): None
Convenience: Inserted before intercourse and left in place at least six hours after; can be left in place for 24 hours, with additional spermicide for repeated intercourse.
Availability: Prescription

Lea's Shield

FDA Approval Date: 2002
Description: A dome-shaped rubber disk with a valve and a loop that is held in place by the vaginal wall. Covers the upper vagina and cervix so that sperm cannot reach the uterus. Spermicide is applied before insertion.
Failure Rate (number of pregnancies expected per 100 women per year): 15
Some Risks: Skin irritation, spotting, discomfort (female and male partners), urinary tract infection. Theoretical risk of toxic shock syndrome.
Protection from Sexually Transmitted Diseases (STDs): None
Convenience: Inserted before intercourse and left in place at least 8 hours after; can be left in place for up to 48 hours, with additional spermicide for repeated intercourse.
Availability: Prescription

Cervical Cap with Spermicide

FDA Approval Date: Prentiff Cap--1988; FemCap--2003
Description: A soft rubber cup with a round rim, which fits snugly around the cervix.
Failure Rate (number of pregnancies expected per 100 women per year): Prentiff Cap--17; FemCap--23 (b, d, e)
Some Risks: Irritation and allergic reactions, abnormal Pap test. (c) Risk of toxic shock syndrome, a rare but serious infection, when kept in place longer than recommended.
Protection from Sexually Transmitted Diseases (STDs): None
Convenience: May be difficult to insert; can remain in place for 48 hours without reapplying spermicide for repeated intercourse.
Availability: Prescription

Sponge with Spermicide

FDA Approval Date: 1983 (Not currently marketed)
Description: A disk-shaped polyurethane device containing the spermicide nonoxynol-9.
Failure Rate (number of pregnancies expected per 100 women per year): 14-28 (d, e)
Some Risks: Irritation and allergic reactions, difficulty in removal. (c) Risk of toxic shock

syndrome, a rare but serious infection, when kept in place longer than recommended.
Protection from Sexually Transmitted Diseases (STDs): None
Convenience: Inserted before intercourse and protects for repeated acts of intercourse for 24 hours without additional spermicide; must be left in place for at least six hours after intercourse; must be removed within 30 hours of insertion. Is discarded after use.
Availability: Nonprescription; not currently marketed

Spermicide Alone

FDA Approval Date: Use started before premarket approval was required. Since November 2002, only one active ingredient has been allowed.
Description: A foam, cream, jelly, film, suppository, or tablet that contains nonoxynol-9, a sperm-killing chemical
Failure Rate (number of pregnancies expected per 100 women per year): 20-50 (studies have shown varying effectiveness rates)
Some Risks: Irritation and allergic reactions, urinary tract infections (c)
Protection from Sexually Transmitted Diseases (STDs): None
Convenience: Instructions vary; check labeling. Inserted between 5 and 90 minutes before intercourse and usually left in place at least six to eight hours after.
Availability: Nonprescription

Oral Contraceptives--combined pill

FDA Approval Date: First in 1960; most recent in 2003
Description: A pill that suppresses ovulation by the combined actions of the hormones estrogen and progestin. A chewable form was approved in November 2003.
Failure Rate (number of pregnancies expected per 100 women per year): 1-2
Some Risks: Dizziness; nausea; changes in menstruation, mood, and weight; rarely, cardiovascular disease, including high blood pressure, blood clots, heart attack, and strokes
Protection from Sexually Transmitted Diseases (STDs): None
Convenience: Must be taken on daily schedule, regardless of frequency of intercourse. Women using the chewable tablet must drink 8 oz. of liquid immediately after taking.
Availability: Prescription

Oral Contraceptives--progestin-only minipill

FDA Approval Date: 1973
Description: A pill containing only the hormone progestin that reduces and thickens cervical mucus to prevent the sperm from reaching the egg.
Failure Rate (number of pregnancies expected per 100 women per year): 2
Some Risks: Irregular bleeding, weight gain, breast tenderness, less protection against ectopic pregnancy
Protection from Sexually Transmitted Diseases (STDs): None
Convenience: Must be taken on daily schedule, regardless of frequency of intercourse.
Availability: Prescription

Oral Contraceptives--91-day regimen (Seasonale)

FDA Approval Date: 2003
Description: A pill containing estrogen and progestin, taken in 3-month cycles of 12 weeks of active pills followed by one week of inactive pills. Menstrual periods occur during the 13th week of the cycle.
Failure Rate (number of pregnancies expected per 100 women per year): 1-2
Some Risks: Similar to oral contraceptives--combined pill
Protection from Sexually Transmitted Diseases (STDs): None
Convenience: Must be taken on daily schedule, regardless of frequency of intercourse. Since users will have fewer periods, they should consider the possibility that they might be

pregnant if they miss scheduled periods. May have more unplanned bleeding and spotting between periods than with 28-day oral contraceptives.
Availability: Prescription

Patch (Ortho Evra)

FDA Approval Date: 2001
Description: Skin patch worn on the lower abdomen, buttocks, or upper body that releases the hormones progestin and estrogen into the bloodstream.
Failure Rate (number of pregnancies expected per 100 women per year): 1-2 (Appears to be less effective in women weighing more than 198 pounds.)
Some Risks: Similar to oral contraceptives--combined pill
Protection from Sexually Transmitted Diseases (STDs): None
Convenience: New patch is applied once a week for three weeks. Patch is not worn during the fourth week, and woman has a menstrual period.
Availability: Prescription

Vaginal Contraceptive Ring (NuvaRing)

FDA Approval Date: 2001
Description: A flexible ring about 2 inches in diameter that is inserted into the vagina and releases the hormones progestin and estrogen.
Failure Rate (number of pregnancies expected per 100 women per year): 1-2
Some Risks: Vaginal discharge, vaginitis, irritation. Similar to oral contraceptives--combined pill
Protection from Sexually Transmitted Diseases (STDs): None
Convenience: Inserted by the woman; remains in the vagina for 3 weeks, then is removed for 1 week. If ring is expelled and remains out for more than 3 hours, another birth control method must be used until ring has been used continuously for 7 days.
Availability: Prescription

Post-Coital Contraceptives (Preven and Plan B)

FDA Approval Date: 1998-1999
Description: Pills containing either progestin alone or progestin plus estrogen
Failure Rate (number of pregnancies expected per 100 women per year): Almost 80 percent reduction in risk of pregnancy for a single act of unprotected sex
Some Risks: Nausea, vomiting, abdominal pain, fatigue, headache
Protection from Sexually Transmitted Diseases (STDs): None
Convenience: Must be taken within 72 hours of having unprotected intercourse.
Availability: Prescription

Injection (Depo-Provera)

FDA Approval Date: 1992
Description: An injectable progestin that inhibits ovulation, prevents sperm from reaching the egg, and prevents the fertilized egg from implanting in the uterus.
Failure Rate (number of pregnancies expected per 100 women per year): less than 1
Some Risks (serious medical risks from contraceptives are rare): Irregular bleeding, weight gain, breast tenderness, headaches
Protection from Sexually Transmitted Diseases (STDs): None
Convenience: One injection every three months.
Availability: Prescription

Injection (Lunelle)

FDA Approval Date: 2000
Description: An injectable form of progestin and estrogen

Failure Rate (number of pregnancies expected per 100 women per year): less than 1
Some Risks: Changes in menstrual cycle, weight gain. Similar to oral contraceptives--combined.
Protection from Sexually Transmitted Diseases (STDs): None
Convenience: Injection given once a month.
Availability: Prescription

Implant (Norplant)

FDA Approval Date: 1990
Description: Six matchstick-sized rubber rods that are surgically implanted under the skin of the upper arm, where they steadily release the contraceptive steroid levonorgestrel.
Failure Rate (number of pregnancies expected per 100 women per year): less than 1
Some Risks: Irregular bleeding, weight gain, breast tenderness, headaches, difficulty in removal
Protection from Sexually Transmitted Diseases (STDs): None
Convenience: Implanted and removed by health-care provider in minor outpatient surgical procedure; effective for up to five years.
Availability: Prescription. In July 2002, Norplant's manufacturer announced that it will no longer distribute the Norplant system. Women using the system should contact their doctors about what their contraceptive options will be after the five-year expiration date of their Norplant systems.

IUD (Intrauterine Device)

FDA Approval Date: 1976 (f)
Description: A T-shaped device inserted into the uterus by a health professional.
Failure Rate (number of pregnancies expected per 100 women per year): less than 1
Some Risks: Cramps, bleeding, pelvic inflammatory disease, infertility, perforation of uterus
Protection from Sexually Transmitted Diseases (STDs): None
Convenience: After insertion by physician, can remain in place for up to one or 10 years, depending on type.
Availability: Prescription

Periodic Abstinence

FDA Approval Date: N/A
Description: To deliberately refrain from having sexual intercourse during times when pregnancy is more likely.
Failure Rate (number of pregnancies expected per 100 women per year): 20
Some Risks: None
Protection from Sexually Transmitted Diseases (STDs): None
Convenience: Requires frequent monitoring of body functions (for example, body temperature for one method).
Availability: Instructions from health-care provider

Trans-abdonimal Surgical Sterilization--female (Falope Ring, Hulka Clip, Filshie Clip)

FDA Approval Date: Early 1970s (g)
Description: The woman's fallopian tubes are blocked so the egg and sperm can't meet in the fallopian tube, preventing conception. (h)
Failure Rate (number of pregnancies expected per 100 women per year): less than 1
Some Risks: Pain, bleeding, infection, other post-surgical complications, ectopic (tubal) pregnancy.
Protection from Sexually Transmitted Diseases (STDs): None
Convenience: One-time surgical procedure that requires an abdominal incision.

Availability: Surgery

Sterilization Implant--female (Essure System)

FDA Approval Date: 2002
Description: Small metallic implant that is placed into the fallopian tubes. The device works by causing scar tissue to form, blocking the fallopian tubes and preventing conception. (h)
Failure Rate (number of pregnancies expected per 100 women per year): less than 1
Some Risks: Mild to moderate pain after insertion, ectopic (tubal) pregnancy.
Protection from Sexually Transmitted Diseases (STDs): None
Convenience: Minor surgical procedure, permanent sterilization. Device is inserted through the vagina using a catheter. Women must rely on another birth control method during the first three months, until placement is confirmed with an X-ray procedure.
Availability: Prescription

Surgical Sterilization--male

FDA Approval Date: N/A
Description: Sealing, tying, or cutting a man's vas deferens so that the sperm can't travel from the testicles to the penis. (h)
Failure Rate (number of pregnancies expected per 100 women per year): less than 1
Some Risks (serious medical risks from contraceptives are rare): Pain, bleeding, infection, other minor postsurgical complications
Protection from Sexually Transmitted Diseases (STDs): None
Convenience: One-time surgical procedure.
Availability: Surgery

(a) Projected from six-month study and adjusted for use of emergency contraception.

(b) If spermicides are used with barrier methods, be sure that the spermicide is compatible with the condom or diaphragm (won't cause it to weaken or break). Oil-based lubricants (such as petroleum jelly or baby oil) will cause latex to weaken and should not be used with these methods.

(c) Spermicides used alone, with barrier devices, or with condoms can cause irritation to the skin lining the vagina, especially when the spermicide is used frequently. There is a possibility that spermicide might increase the risk of acquiring some sexually transmitted diseases because of disruption of the vaginal skin. Spermicide has not been proven to be effective against bacteria and viruses in people. Therefore, there is no reason to use spermicide during pregnancy.

(d) Medications for vaginal yeast infections may decrease effectiveness of spermicides.

(e) Less effective for women who have had a baby because the birth process stretches the vagina and cervix, making it more difficult to achieve a proper fit.

(f) First approval date of currently marketed IUDs. Some IUDs were sold before premarket approval was required. Those products are no longer on the market.

(g) Sold before premarket approval was required (1976).

(h) A contraceptive option for people who don't want children. Considered permanent because reversal is typically unsuccessful.

(Source: Food and Drug Administration 12/03)

Return to Main Article

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FDA Office of Public Affairs
FDA Consumer Magazine

Megestrol

(me jess' trole)

Brand name(s): Megace

Contents of this page:

About your treatment

Your doctor has ordered the drug megestrol to help treat your illness. Megestrol comes as tablets and as a liquid to take by mouth.

This medication is used to treat:

- metastatic breast cancer
- metastatic endometrial cancer

This medication is sometimes prescribed for other uses; ask your doctor or pharmacist for more information.

Megestrol is similar to progesterone, a hormone produced by the body. It is not known how megestrol prevents cancer cell growth or how it stimulates appetite.

Other uses for this medicine

Megestrol also is used to stimulate appetite and promote weight gain in patients with muscle wasting due to cancer or in patients with acquired immunodeficiency syndrome (AIDS). Megestol has been used with estrogen to prevent pregnancy. It also has been used in the treatment of prostatic hypertrophy, endometriosis, and endometrial hyperplasia. Talk to your doctor about the possible risks of using this drug for your condition.

Precautions

Before taking megestrol,

- tell your doctor and pharmacist if you are allergic to megestrol or any other drugs.
- tell your doctor and pharmacist what prescription and nonprescription medications you are taking, especially

aspirin and vitamins.
- tell your doctor if you have or have ever had diabetes, a stroke, or a blood clot.
- do not take megestrol if you are pregnant, plan to become pregnant, or are breast-feeding. If you become pregnant, call your doctor immediately. Megestrol may harm the fetus.
- you should know that megestrol may interfere with the normal menstrual cycle (period) in women and may stop sperm production in men. However, you should not assume that you cannot get pregnant or that you cannot get someone else pregnant. Women who are pregnant or breast-feeding should tell their doctors before they begin taking this drug. You should not plan to have children while receiving chemotherapy or for a while after treatments. (Talk to your doctor for further details.) Use a reliable method of birth control to prevent pregnancy.

Side effects

Although side effects from megestrol are not common, they can occur. Tell your doctor if any of these symptoms are severe or do not go away:

- increased appetite and weight gain
- swelling of the hands, feet, or lower legs
- increased sugar level in the blood
- headache
- breast tenderness
- impotence
- decreased sexual desire
- increase in blood pressure

If you experience any of the following symptoms, call your doctor immediately:

- nausea or vomiting
- dizziness
- weakness
- leg pain
- breathing discomfort
- unusual bleeding or bruising
- rapid heartbeat
- chest pain
- cough
- sore throat
- weakness or numbness of an arm or leg
- sharp, crushing chest pain or heaviness in chest
- sudden shortness of breath
- severe mental depression
- unusual bruising or bleeding

Storage conditions

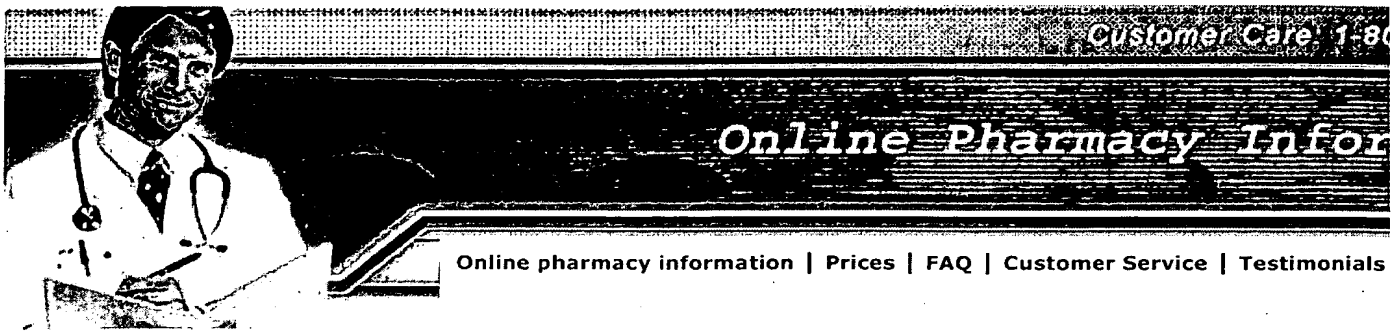
Keep megestrol in the container it came in, tightly closed, and out of reach of children. Store it at room temperature and away from excess heat and moisture (not in the bathroom). Throw away any medication that is outdated or no longer needed. Talk to your pharmacist about the proper disposal of your medication.

In case of emergency/overdose

In case of overdose, call your local poison control center at 1-800-222-1222. If the victim has collapsed or is not breathing, call local emergency services at 911.

Last Revised - 01/01/2003

American Society of Health-System Pharmacists, Inc. Disclaimer



DIET PILLS
WEIGHT LOSS

Phentermine Adipex
Ionamin Bontril
Meridia Xenical
Didrex Tenuate
Phendimetrazine
Diethylproprion

PAIN RELIEF

Celebrex Vioxx
Ultram Imitrex
Tramadol Ultracet
Fioricet Mobic
Bextra

MEN'S HEALTH

Propecia Viagra
Levitra

WOMEN'S HEALTH

Ortho Tri-Cyclen Triphasil
Ortho Evra patch Estradiol
Nordette 28 Diflucan

SKIN CARE

Retin-A Renova
Vaniqa

STOP SMOKING

Zyban

SEXUAL HEALTH

Valtrex Acyclovir
Aldara Famvir
Condylox Denavir
Zovirax

MUSCLE RELAXANTS

Cyclobenzaprine Skelaxin
Zanaflex Flexeril
Carisoprodol (Soma)

ALLERGY RELIEF

Allegra Flonase
Zyrtec Nasacort
Nasonex

ANTI-DEPRESSANTS

Paxil Prozac
Zoloft Effexor
Wellbutrin Celexa

ANXIETY

Buspar Buspirone

Ortho tri-cyclen

Ortho Tri-Cyclen is an estrogen and progestin combination used to prevent pregnancy. It may also be used to regulate the menstrual cycle, treat symptoms of menopause, or treat other conditions as determined by your doctor.

Cheapest Price

Online ortho tri-cyclen information

Product	Qty	Price	Shipping
Ortho Tri-Cyclen	1	$87.00	$18.00
Ortho Tri-Cyclen	3	$197.00	$18.00

Ortho Tri-Cyclen online

(Birth Control - Oral)

Possible uses of this medication

Ortho Tri-Cyclen is an estrogen and progestin combination used to prevent pregn be used to regulate the menstrual cycle, treat symptoms of menopause, or treat as determined by your doctor.

How to take this medication

Follow the directions for using this medicine provided by your doctor. This medici patient information leaflet. Read it carefully. Ask your doctor, nurse, or pharmacis that you may have before using this medicine. Try to take this medicine at the sa day, not more than 24 hours apart. Store this medicine at room temperature, aw light. If you miss a dose of this medicine, take it as soon as you remember. Take the regular time. This means you may take 2 doses on the same day. If you miss dose of this medicine, refer to the patient information that came with this medicir any questions, contact your doctor, nurse, or pharmacist.

Side Effects

Side effects, that may go away during treatment, include nausea, vomiting, bleed menstrual periods, breast tenderness, or weight change. If they continue or are b check with your doctor. Check with your doctor as soon as possible if you experie recurrent abnormal vaginal bleeding, a missed menstrual period, dizziness or fain fingers or ankles, headache, or difficulty wearing contact lenses. Contact your doc if you experience sharp or crushing chest pain, sudden shortness of breath, sudde headache or leg pain, yellow skin or eyes, changes in vision, numbness of an arm stomach pain. If you notice other effects not listed above, contact your doctor, nu pharmacist.

SLEEPING AIDS

Sonata Ambien

STOMACH

Prilosec Nexium
Protonix Aciphex

Precautions

Smoking cigarettes while using this medicine may increase your risk of stroke, he clots, high blood pressure, or other diseases of the heart and blood vessels. If yo or diarrhea for any reason, your medicine may not work as well. Taking certain a anticonvulsants while you are using this medicine may decrease the effectiveness To prevent pregnancy, use an additional form of birth control until your next peri any questions, contact your doctor, nurse, or pharmacist. Before you have any m treatments, emergency care, or surgery, tell the doctor or dentist that you are us If you wear contact lenses and you develop problems with them, contact your do begin taking any new medicine, either prescription or over-the-counter, check wit pharmacist. This medicine may cause dark skin patches on your face. Exposure t make these patches darker. If patches develop, use a sunscreen or protective clo exposed to the sun, sunlamps, or tanning booths. Use of this medicine will not pr of sexually transmitted diseases (STDs). Do not use this medicine if you are preg suspect that you could be pregannt, contact your doctor immediately. This medici breast milk. If you are or will be breast-feeding while you are using this medicine, doctor or pharmacist to discuss the risks to your baby.

Drug Interactions

Tell your doctor of all nonprescription and prescription medication you may use, e nitrate medications (e.g., nitroglycerin, isosorbide dinitrate), nitroprusside (any "n donor" medicines), cimetidine, erythromycin, azole antifungals (e.g., itraconazole mibefradil, rifamycins (e.g., rifampin) or high blood pressure medicines.

Missed Dose

If you miss a dose, do not double the next dose. Instead, skip the missed dose a usual dosing schedule.

Storage

Store at room temperature away from light and moisture. Keep this and all medic reach of children.

Notes

DO NOT SHARE THIS MEDICINE with others for whom it was not prescribed. DO N MEDICINE for other health conditions. KEEP THIS MEDICINE out of the reach of c THIS MEDICINE FOR AN EXTENDED PERIOD OF TIME, obtain refills before your s